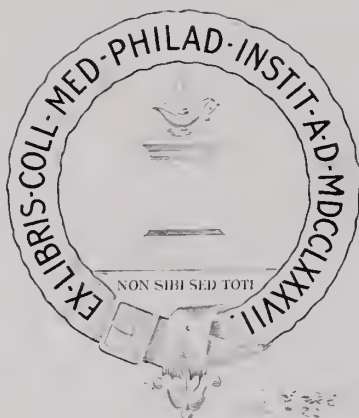


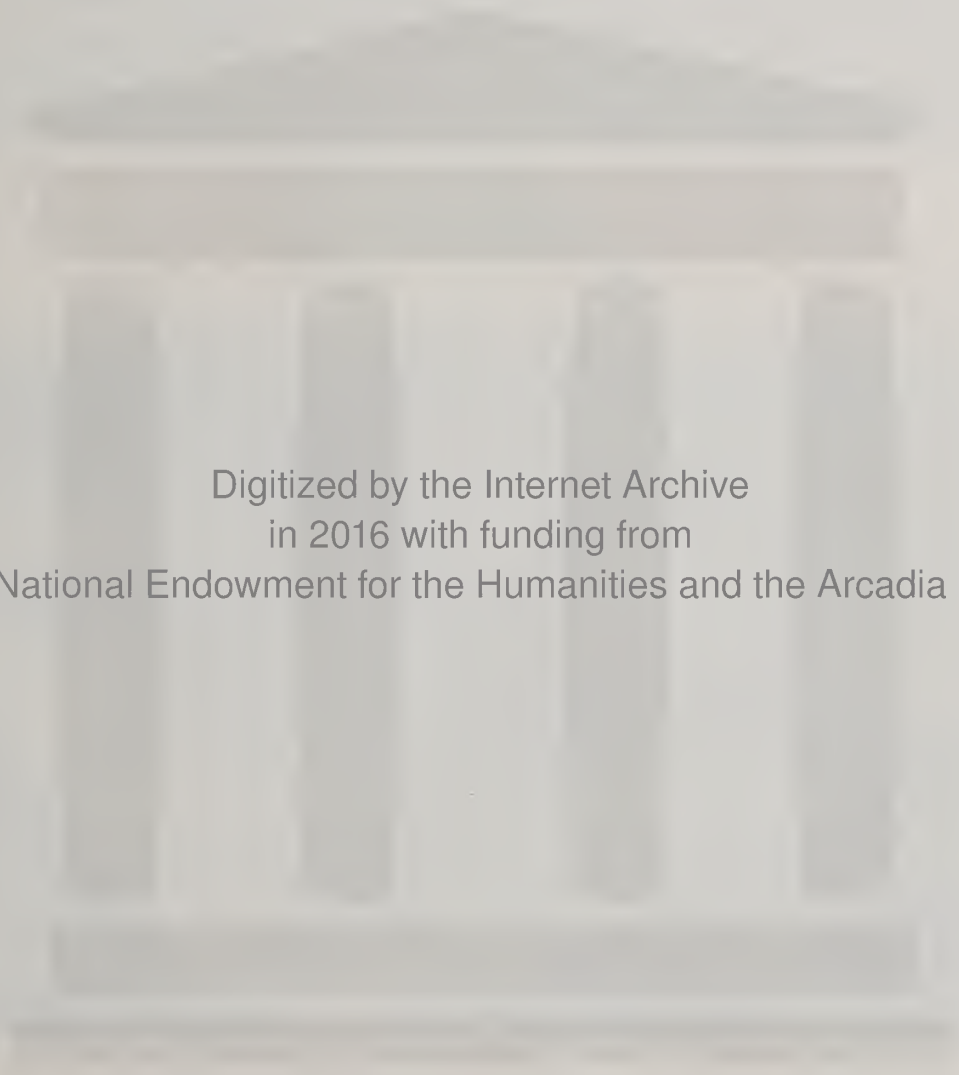


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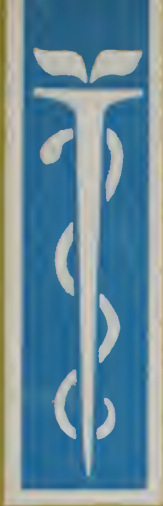
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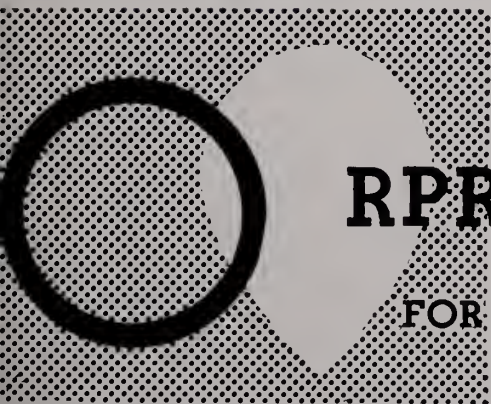
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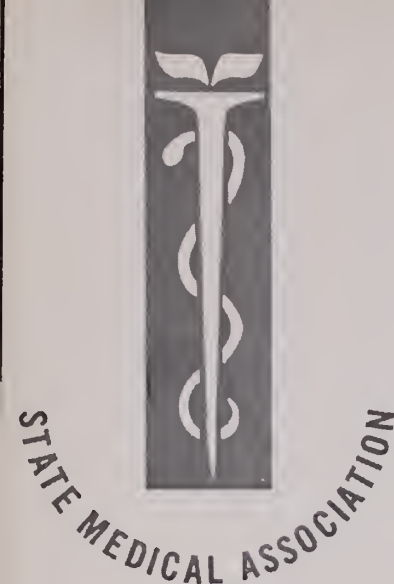
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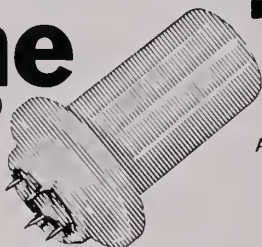
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President's Letter

MY "MAIDEN EFFORT" at writing this President's letter to all of you concerns a subject which should be of great interest to each of us. I am referring to the debate which is currently going on regarding the real value of our annual MSMA meeting in May. The attendance has been dropping off the last few years, and the meeting was cut from three days to two.

There is no doubt in all of our minds, however, that some overhauling is due. There are two committees of your association which are working on this problem. One of them is the ongoing Permanent Evaluation Committee, whose Chairman is Past President Haddon Carryer of Rochester. This committee has recommended a two and one-half day session, rather than the shorter two day meeting. The House of Delegates will meet on Sunday, as usual, and again on Tuesday for its final session. There will be committee breakfasts on Monday, Tuesday, and Wednesday mornings, where desired.

The other committee, which has put much time and thought into the program section, is the Committee on Scientific Assembly. It has come up with a whole format for this coming May meeting. The reasons for this are many. There is much more competition today than in years past for the physician's time spent in postgraduate study. There are at least two other very excellent meetings held near the time of the State Meeting, with which we must compete. This competition is good for us, as we are being forced, as it were, into creating a better meeting.

Your Committee on Scientific Assembly

has made several big changes. There will be seven major topics discussed in depth, for one to one-and-a-half hours each, with time for questions. There will be the usual break between sessions for viewing of the scientific and commercial exhibits. There will be one entirely new (to many of us, at least) period with 10 short subjects being presented at 5 minutes each. These will be "tricks of the trade" talks entitled "How to do it" topics such as the plugged catheter, the bloody nose, warts, etc. These are the common "garden variety" problems which most of us see every day, and which can be very vexing to handle.

Dr. Arthur C. Aufderheide and some of his colleagues in Duluth are going to innovate a program on Erythroblastosis which will involve some preliminary study by those who are interested and sign up for the course in advance of the meeting. The possibilities offered here sound exciting, indeed.

The last session, Wednesday morning, will be devoted to the Socio-Economics of Medicine, which are of such great interest to all of us today. This program has not been worked out, as it is much too early to do so. Our own State Legislature, as well as the 90th United States Congress are now in session, and events can change rapidly in this area. For this reason no agenda can be worked out that would be meaningful, until the last minute.

All of your officers, councilors, and committees urge you to attend as many of the sessions as you can; we want you to see that

Continued on page 48

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Criminal Abortion

Deaths
and
Suicides
in
Pregnancy
in
Minnesota,
1950-1964*

ALEX BARNO, M.D.
St. Louis Park, Minnesota

BECAUSE THE recent lay and medical literature^{1,2,3} is being bombarded with the repetitious figure of 5,000-10,000 deaths annually in the United States from criminal abortion, it was decided to test the reality of this figure as it pertains to the State of Minnesota. Also, since the most frequent psychiatric indication for therapeutic abortion is the fear of the patient committing suicide, the problem of suicide in pregnancy is included in this report. The material herein is from the Minnesota Maternal Mortality Study for the 15-year period, 1950 through 1964. The mechanics of the study need not be repeated since it is known to the physicians of the state. This has been a continuous study since 1950 and previous reports have been published.

Criminal Abortion Deaths

During the period of this study there have been on the average 4,000,000 live births annually in the United States, to which Minnesota has contributed an average of 80,000 annually, or 1/50th of the total. As has been reported, the crusaders for the liberalization of therapeutic abortion have published the repetitious figures of 1,000,000-1,500,000 criminal abortions being done annually in the United States with 5,000-10,000 deaths resulting. If Minnesota contributes 1/50th of the birth rate annually, it should contribute 1/50th of the annual criminal abortion deaths. One fiftieth of 5,000 is 100 and 1/50th of 10,000 is 200. However, as will be shown later, instead of 100-200 criminal abortion deaths annually in Minnesota, there have been 20 in 15 years or 1 per year. Where are the other 99 or 198? We can't find them in the Minnesota

*From the Minnesota Maternal Mortality Study.

Part of the Symposium on Therapeutic Abortion read at the meeting of the Minnesota Obstetrical and Gynecological Society, Rochester, April 23, 1966.

Requests for reprints should be addressed to the St. Louis Park Medical Center, 4959 Excelsior Blvd., Minneapolis, Minnesota.

Maternal Mortality Study, which is as accurate a study as any in the nation. There is no doubt that we are missing some, but we certainly are not missing 99 or 198 per year. What is the source of these figures being reported? The physician and lay criminal abortionists have not published their figures as yet. Therefore, either the professional competence of the criminal

abortionists has been seriously underestimated or else these figures have been grossly exaggerated. The latter seems the more probable. In any event, the death rate due to illegal abortion can be decreased only by allowing legal abortion to any woman who asks for it. But most physicians certainly would see no medical reason to do so.

In Table 1 are shown the Minnesota Maternal Mortality rates and preventability for 1941 and the years under discussion. Since 1960 the live births have decreased yearly. The corrected maternal mortality rate has remained at 0.1 to 0.2 per 1000 live births during the last eight years, which seems to be an irreducible minimum and speaks well for the physician care of the obstetric patient.

Infection and Air Embolism

Table 2 summarizes the 370 obstetric causes of death. The criminal abortions are in the infection and air embolism categories. The totals for each category were 11 and nine respectively. These will be discussed subsequently in more detail. Of the 11 air embolism deaths, two were due to air being pumped in under pressure during blood transfusion by R.N. anesthetists at surgery.

TABLE 1
Minn. Maternal Mortality Rates and Preventability,
1941, 1950-1964

Year	Live Births	Total Mat. Deaths	Gross Mort. Per 1,000 Live Births		Corrected Mort. Rate	Preventability % of Total Mat. Deaths	
			Ob-	stetric		No.	Deaths
1941	55,293	112	2.03	93	1.68	82	73
1950	76,074	68	0.89	47	0.62	22	32
1951	80,099	57	0.71	39	0.45	24	42
1952	78,990	58	0.73	31	0.39	10	17
1953	79,362	59	0.74	33	0.42	15	25
1954	81,033	40	0.49	27	0.33	12	30
1955	81,665	43	0.53	31	0.38	8	16
1956	82,620	45	0.54	26	0.31	10	22
1957	86,019	60	0.70	21	0.24	7	12
1958	85,594	26	0.33	14	0.16	3	12
1959	87,724	37	0.42	21	0.24	7	19
1960	88,126	29	0.33	17	0.19	6	21
1961	85,954	27	0.31	17	0.20	7	26
1962	83,911	29	0.35	14	0.17	3	10
1963	79,775	16	0.20	13	0.16	3	19
1964	75,599	36	0.48	19	0.25	7	19

TABLE 2
Obstetric Causes of Death and Preventability, 1950-1964

Cause of Death	No.	%	Prev.	% of Total Prev. Deaths
Hemorrhage	99	27	60	43
Infection	68	18	17	12
Toxemia	58	16	22	16
Heart disease	36	10	8	6
Amniotic fluid embolism	27	7	0	0
Anesthesia	16	4	11	8
Chorionepithelioma	15	4	0	0
Air embolism	11	3	6	4
Others	40	11	14	10
Not determinable (12)	—	—	—	—
Transfusion deaths (7)	—	—	—	—
Dehydration and electrolyte imbalance (5)	—	—	—	—
Diabetes mellitus (5)	—	—	—	—
Idiopathic pulmonary edema (4)	—	—	—	—
Suicide (post-partum psychosis) (3)	—	—	—	—
Pituitrin shock (2)	—	—	—	—
Overhydration with water intoxication (1)	—	—	—	—
Unexplained shock (1)	—	—	—	—
Totals	370	100	138	99

The other nine were criminal abortions (catheter inserted into the uterus). All of them had autopsies.

Suicides

Under "others" category are listed three suicides from post-partum psychosis. During the first few years of the study the Maternal Mortality Committee tried to assess psychiatric disease as obstetrical versus non-obstetrical. If the mental aberration occurred before pregnancy the disease was assessed as non-obstetrical. If it occurred during pregnancy or post partum, the disease was assessed as obstetrical. This concept was later discontinued and all the suicides were included in the trauma category as violent deaths in the non-obstetric causes.

For completeness the 260 non-obstetric causes of death are tabulated in Table 3. The other 11 suicides are included in the trauma category. Thus there were a total of 630 maternal deaths among 1,232,545 live births during the 15 years under consideration.

Illegitimate Live Births vs. Illegitimate Maternal Deaths

Table 4 correlates the illegitimate live births with illegitimate maternal deaths. The illegitimate live births have more than doubled during the last 15 years. Are we going to solve this problem by aborting all of them as some would advocate? Psychiatrists, psychologists, social workers, theologians, parents and others have been groping with this problem since the beginning of time and it is still with us. If all 3,655 illegitimate live births had been aborted therapeutically early in pregnancy in 1964, it would be safe to assume that there would have been twice this number to perform in 1965.

There were a total of 38 maternal deaths among 33,620 illegitimate live births with 11 of these being criminal abortion deaths. These are analyzed in more detail in Table 5. The criminal abortions comprised one half of the obstetrical causes of death. A word is in order regarding the four homicides under the non-obstetrical causes. Two of these were perpetrated by the consort because

the patient refused to marry him; one was perpetrated by the consort because he refused to marry her; and the other case was a divorcee who accused a married man of being the father of the child with the result that she was strangled by him.

Table 6 is a breakdown of all of the criminal abortion deaths. These were almost equally divided between the illegitimate and legitimate pregnancies. As to causes, they were also almost equally divided between

TABLE 3
Non-Obstetric Causes of Death, 1950-1964

Cause	No.
Trauma	45
Malignant tumors	36
Intracranial hemorrhage	27
Poliomyelitis	25
Not determinable	19
Asian flu	16
Peritonitis	13
Infectious hepatitis	8
Pneumonia	7
Leukemia	6
Glomerulonephritis	5
Coronary occlusion	4
Lupus erythematosus	4
Panmyelophthisis	4
Pyelonephritis	4
Meningitis	3
Dissecting aneurysm of aorta	3
Acute alcoholism	2
Ruptured aneurysm of splenic artery	2
Status asthmaticus	2
Spontaneous hemothorax	1
Insulin coma	1
Obstructed laryngo-tracheitis	1
Hereditary cystic disease of liver	1
Ruptured multiple pulmonary aneurysms	1
Hemorrhage from liver abscess	1
Hemorrhage at attempted liver transplant	1
Acute rheumatic fever	1
Shock of undetermined origin	1
Bilateral spontaneous pneumothorax	1
Hypersplenism	1
Pulmonary tuberculosis	1
Obstruction of trachea	1
Thrombocytopenic purpura	1
Brain abscess	1
Status epilepticus	1
Spontaneous rupture of thoracic aorta	1
Acute cerebral edema	1
Pulmonary aspiration of stomach contents	1
Tetanus	1
Cirrhosis of liver	1
Acute pulmonary edema	1
Infarction of G.I. tract	1
Epidural abscess	1
Acute pancreatitis	1
Total	260

TABLE 4
Illegitimate Live Births and Maternal Deaths
in Minnesota, 1950-1964

Year	Illeg. Births	Rate Per 1000 Live Births	Maternal Deaths	Criminal Abortions
1950	1696	22.5	3	0
1951	1600	20.0	4	0
1952	1530	19.3	2	2
1953	1620	20.5	3	1
1954	1833	22.7	5	1
1955	1810	22.3	3	0
1956	1941	23.5	3	0
1957	2053	24.0	2	0
1958	2108	24.9	2	1
1959	2321	26.3	2	2
1960	2525	28.8	1	0
1961	2737	31.6	1	1
1962	2965	34.9	3	0
1963	3226	40.1	3	2
1964	3655	47.3	1	1
Total	33,620		38	11

TABLE 5
Analysis of Illegitimate Maternal Deaths
in Minnesota, 1950-1964

Obstetrical causes		22
Criminal abortions	11	
Septic abortions (6)		
Air embolism (5)		
Septic abortion	1	
Toxemia	2	
Hemorrhage (retained placenta)	2	
Hemorrhage (ruptured ectopic)	1	
Transfusion death (overload)	1	
Amniotic fluid embolism	1	
Chorionepithelioma	1	
Anesthetic death	1	
Unknown	1	
Non-obstetrical causes		16
Homicide	4	
Auto accident	2	
Brain tumor	2	
Acute alcoholism	2	
Coronary occlusion	1	
Infectious hepatitis	1	
Virus pneumonia	1	
Dissecting aneurysm of aorta	1	
Irreversible insulin coma	1	
Pulmonary aspiration of stomach contents	1	
Total		38

TABLE 6
Total Criminal Abortion Deaths in Minnesota, 1950-1964

Septic abortion		11
Illegitimate	6	
Legitimate	5	
Air embolism		9
Illegitimate	5	
Legitimate	4	
Total		20

septic abortion and air embolism. Thus there were a total of 20 among 1,232,545 live births or one per every 61,627 live births. It is interesting to note the method used for the abortions. In seven instances the catheter was used; in seven the method was unknown. The other methods were as follows: rubber tubing, syringe with solution of soap and turpentine, glass straw with bulb syringe and soap and turpentine, plastic tube with soap solution, tap water douche under high pressure and nut pick. The bacteriology of the septic abortion deaths has been published previously.⁴

Suicides

As the medical indications for therapeutic abortion have dwindled to almost nothing, the psychiatric indications have risen. Simon⁵ states that as many as 80 per cent of therapeutic abortions are for psychiatric reasons. Gold⁶ from New York City for a three-year period, 1960-1962, reported that 61 per cent of the therapeutic abortions were done for psychiatric indications. Since the principal criterion for psychiatric recommendation is the likelihood of suicide, it was decided to investigate the reality of this from the Maternal Mortality data.

Table 7 shows the deaths and death rates due to suicide in Minnesota residents. As can be seen, males kill themselves four to five times more frequently than females. There were a total of 14 suicides in the obstetrical patient. Not a single one of these women was illegitimately pregnant. Not a single one requested a therapeutic abortion. Suicide in pregnancy is rare — 0 to 0.1 per 100,000 population. Expressed in another manner, there were 14 among 1,232,545 live births or one per every 88,035 live births, slightly less than one per year. Perhaps pregnancy has a psychically protective role.

As explained earlier in this paper, most of the suicides (11) were placed in the trauma category (Table 8). With the other three in the obstetrical category, this made a total of 14. The other trauma deaths are self explanatory.

Table 9 shows a more detailed analysis of the 14 suicides. Regarding parity, four

CRIMINAL ABORTION — BARNO

were primigravidas and the remainder multiparas. It is interesting to note that 10 committed suicide post partum and only four with the fetus in utero, or one per every 308,136 live births. The fetus in utero must be a protective mechanism; it is conceivable that women are reluctant to take another life with them. A psychiatrist-consultant, after studying the 14-case history protocols, made the diagnoses as listed. There were 12 psychotic depressions and two schizophrenics. Only four of the total of 14 had seen a psychiatrist for help. The family, the family physician and the obstetrician were remiss in seeking psychiatric help. The method of suicide is tabulated and is self-explanatory.

Other studies have also shown that suicide in pregnancy occurs rarely. Höök⁷ in Sweden in 1963 published a 7½-11-year follow-up study of 249 women who in 1948 were refused a legal abortion. Of the 249, 86 per cent continued the pregnancy and delivered, 3 per cent had a spontaneous abortion and 11 per cent had an illegal abortion. There were no suicides or suicide attempts in any of these even though seven had attempted suicide in the non-pregnant state.

How can pregnancy cause such a psychiatric upheaval or turmoil as to alter the psychodynamics of an individual to the extent that she will commit suicide? If she does not do so, psychiatrists tell us that she will be very unhappy or upset. This

seems a most nebulous, non-objective, non-scientific approach to medicine. Are we all happy and serene all of the time or even

TABLE 7
Deaths and Death Rates Due to Suicide,
Minnesota Residents, 1950-1964

Year	Number of Deaths				Rate Per 100,000 Population		
	Total	Male	Fe- male	Preg- nant Female	Male	Female	Preg- nant Female
1950	351	291	60	3	19.4	4.1	0.2
1951	291	233	58	0	15.3	3.9	0.
1952	306	254	52	1	16.5	3.4	0.07
1953	302	239	63	3	15.3	4.1	0.2
1954	312	258	54	1	16.4	3.4	0.06
1955	297	246	51	0	15.4	3.2	0.
1956	304	246	58	1	15.2	3.6	0.06
1957	296	246	50	2	15.0	3.0	0.12
1958	300	245	55	1	14.8	3.3	0.06
1959	319	266	53	0	15.9	3.1	0.
1960	334	265	69	1	15.7	4.0	0.06
1961	323	266	57	0	15.5	3.3	0.
1962	343	261	82	0	15.1	4.7	0.
1963	371	285	86	0	16.2	4.8	0.
1964	358	265	93	1	15.2	5.2	0.06

TABLE 8
Trauma Deaths in the Obstetrical Patient
in Minnesota, 1950-1964

Cause	No.	%
Auto accident	23	51
Suicide	11	24
Homicide	5	11
Accidental burns	3	7
Accidental drowning	2	4
Suffocation — etiology unknown	1	2
Total	45	99

TABLE 9
Suicide in the Obstetrical Patient in Minnesota, 1950-1964

No.	Age	Parity	Gestation	Psychiatric Diagnosis	Method of Suicide
1.	36	2012	7 wks. p.p.	Schizophrenia	Jumped in front of train
2.	25	0000	3 wks. p.p.	Psychotic depression	Drowning
3.	39	3003	2½ mo. p.p.	Psychotic depression	Hanging
4.	26	1001	2 mo. p.p.	Psychotic depression	Gunshot
5.	34	0000	2 mo. p.p.	Psychotic depression	Cutting throat
6.	21	0000	11 wks. p.p.	Psychotic depression	Drowning
7.	25	3003	2 wks. p.p.	Psychotic depression	Drowning
8.	30	2002	2 mo. p.p.	Psychotic depression	Auto crash concrete wall
9.	24	2002	6 wks. p.p.	Psychotic depression	Gunshot
10.	37	4004	3 wks. p.p.	Schizophrenia	Gunshot
11.	22	1001	34 wks.	Psychotic depression	Barbiturate
12.	19	0000	32 wks.	Psychotic depression	Barbiturate
13.	29	2012	25 wks.	Psychotic depression	Carbon monoxide
14.	31	Multipara	26 wks.	Psychotic depression	Jumped from 9th floor

most of the time? Isn't there some unhappiness and turmoil in all of our lives? It would seem that the psychiatrists could be accomplishing more by treating or rehabilitating the patient instead of recommending the destruction of another human being. It would also seem that a better solution to this whole problem might be one of prophylaxis — more use of available contraceptive agents and a more liberal sterilization policy.

Summary and Conclusions

1. The Minnesota situation with regard to maternal deaths due to criminal abortion and suicide in pregnancy has been reported for the 15-year period, 1950-1964.

2. The repetitious figures of 1,000,000-1,500,000 criminal abortions annually in the United States with 5,000-10,000 deaths that are bombarding the medical and lay literature are inaccurate. It has been shown that if they were true, Minnesota should be having 100-200 criminal abortion deaths annually. In reality, Minnesota has one criminal abortion death yearly (20 during the 15-year period).

3. As to cause of death, the 20 criminal abortion deaths were almost equally divided between septic abortion and air embolism and between illegitimate and legitimate pregnancies.

4. The death rate due to illegal abortion can be decreased only by allowing legal abortion to any woman who asks for one. Most physicians certainly would see no medical reason for this.

5. As the medical indications for therapeutic abortion have dwindled to almost nothing, the psychiatric indications have risen — 60-80 per cent of those being done at the present time.

6. Psychiatrists use the likelihood of suicide as a danger to the life of the mother as the principal criterion for psychiatric recommendation for therapeutic abortion. This is not being realistic.

7. There were only a total of 14 suicides in the obstetrical patient among 1,232,545 live births or one per 88,039 live births. This was less than one per year. Expressed in another manner, the rate varied from 0 to 0.1 per 100,000 population as compared to 3.1 to 5.2 per 100,000 population of all females.

8. Not a single one of the suicides was illegitimately pregnant and none requested therapeutic abortion.

9. Of the 14 suicides, 10 occurred during the post-partum state and only four with the fetus in utero. Perhaps pregnancy has a psychically protective role.

10. Regarding the psychiatric diagnoses, 12 were psychotic depressives and two were schizophrenics.

11. Only four of the 14 had seen a psychiatrist for help. The family, the family physician and the obstetrician were remiss in seeking psychiatric consultation.

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References

1. Best, Winfield and Jaffee, F. S.: Should Abortion Laws be Liberalized? *Parents Magazine and Better Homemaking*, June, p. 50, 1965.
2. Kummer, J. M. and Leavy, Z.: Therapeutic Abortion Law Confusion. *JAMA* 195:140, 1966.
3. Fisher, R. S.: Criminal Abortion in Rosen, H. (ed.): *Therapeutic Abortion*, New York: The Julian Press, Inc., 1954.
4. Barno, A.: Obstetric Infection Deaths in Minnesota. *Minnesota Med* 47:999 & 1139, 1964.
5. Simon, A.: *Psychiatric Indications for Therapeutic Abortion and Sterilization in Overstreet, E. W. (ed.): Clinical Obstetrics and Gynecology*, New York: Hoeber Medical Division, Harper and Row, March, 1964.
6. Gold, E. M., Erhardt, E. L., Jacobziner, H. and Nelson, F. G.: *Therapeutic Abortions in New York City: A 20-year Review*. *Amer J Public Health* 55:964, 1965.
7. Höök, K.: Refused Abortion. *Acta Psychiat Scand* 39:168, 1963.

On Quaffing

The great Canadian physician Sir William Osler was lecturing one day on alcohol. "Is it true," asked a student, "that alcohol makes people able to do things better?" "No," replied Sir William. "It just makes them less ashamed of doing them badly."

Abortion Laws*

Inequitable,
Inconsistent
and
Hence
Inexcusable

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THE PRESENT practice of performing therapeutic abortions in the United States is inequitable, inconsistent and hence inexcusable. The medical and legal professions share the responsibility for creating this situation and therefore should accept the responsibility for correcting it.¹ It is known that the medical profession cannot and will not dictate abortion policies. Neither can the legal profession dictate abortion policy. It is undeniable that at the present time the abortion laws are flagrantly flouted, much more often for the rich than for the poor. This situation is unacceptable to many practicing physicians since it makes hypocrites out of them and forces them to care for their patients in a manner which many times is in conflict with sound medical practice in many reputable hospitals. Since it is primarily the obstetrician who is concerned with circumventing these antiquated abortion laws it ought to be the obstetrician who should seek their modernization.

Abortion Laws in Minnesota

Minnesota is one of nine states which in its statute mentions that an abortion is allowable if it is performed to save the life of either the mother or the child.² The latter phrase is included because of the concern about abortion prosecutions arising out of instances where a doctor decides that premature labor must be induced.

In 1963 a legislative committee of the state legislature heard the following proposal as part of the Proposed Minnesota Criminal Code Revision, "... that therapeutic abortion be deemed justified when it is performed by a physician and performed in a licensed hospital if any of the following conditions exist: Rape, when it is necessary to save the life of the mother, or avoid grave impairment in the physical or mental condition of

*Part of the Symposium on Therapeutic Abortion read at the meeting of the Minnesota Obstetrical and Gynecological Society, Rochester, April 23, 1966.

the mother, or to prevent the birth of a child with grave physical or mental defects. This procedure should be approved by two other physicians."

Abortion Laws in the United States³

All of the 50 states have statutes indicating severe penalties for criminal abortion. With one or two exceptions, each state has recognized necessity as a justification for therapeutic abortion.*

American Law Institute Proposal

The American Law Institute is a group of eminent jurists, lawyers and professors of law who make occasional proposals to update antiquated laws in the United States. These men are highly respected for their opinions and are adequately qualified to make their recommendations. In 1959, they recommended in their Model Penal Code that abortion laws should be modified.*

Acceptance Proposal by Organized Medicine and the Laity

In 1964 a questionnaire was sent out to 2,285 obstetricians and gynecologists in the state of New York asking for their views on the acceptance or rejection of the American Law Institute proposal as it relates to the performance of therapeutic abortion. The following results were obtained:⁷

Number in favor	1,152	85.3%
Number opposed	198	14.7%
Replies received	1,350	62%

The Committee on Human Reproduction of the American Medical Association recently recommended approval almost verbatim of the Model Penal Code of the American Law Institute.⁸ As a result of the recent California legal action against prominent obstetricians for performing therapeutic abortions, many outstanding obstetricians and lawyers have gone on record as approving a revision of the law. Numerous medical and legal societies have approved such action. The New York Academy of Medicine, The California Medical Association's House of Delegates, The California State Department of Public Health, The California State Board of

Health, the main obstetrics and gynecology societies of California, the Medical Society of the County of New York, the New Jersey Branch of the American Medical Women's Association and many leading obstetricians and gynecologists⁹ in the United States have all urged reform of the law in accordance with the Model Penal Code of the American Law Institute. Professor Nicholson Eastman's⁹ only objection to the American Law Institute proposal is based on the use of the word "believes." He states that a "belief" that an abortion is necessary is not enough and that there exists the possibility that unscrupulous physicians will pervert the law, and he proposes that in addition to the Model Penal Code recommendation a therapeutic abortion committee be established in each hospital and that to this committee be given the responsibility of approving or rejecting the request, in order to prevent the "double standard" in respect to indications for abortion . . . a liberal one for private patients and a much more stringent one for ward patients. Professor Eastman further states that the fact that law enforcement agencies seem to condone the violation of our present abortion laws only serves to stress the inconsistency of the situation.

Unrealistic Laws

It becomes perfectly obvious that these laws are recognized as unrealistic by prominent members of the legal profession as shown by the 1959 recommendation of the American Law Institute. That these laws are felt to be unrealistic by medical groups and individuals seems perfectly clear. That the laity knows these laws to be unrealistic is documented by the fact that 20% of all pregnancies are illegally aborted.^{1,4,5,8} A recent Gallup Poll¹⁰ reported that the effort of the A.M.A. to get states to adopt a uniform and liberalized abortion law is looked upon with favor by a majority of those interviewed. Nearly 80% of adults favored legalizing abortion when a mother's health is endangered and 54% when the child might be born deformed. Substantial majorities of both Catholics and Protestants favored the former; however, when a child might be born with a physical or mental deformity, 46% of Catho-

*See "It's the Law" page 45.

lics and 56% of Protestants were in favor of abortion.

It seems clear that if the medical and legal profession fails to assume the leadership necessary to change the existing laws, it will only be a matter of time before an informed and outraged public will demand the necessary alterations and renovations of the law. People are asking, "How many more women must be sacrificed to needless suffering and death before changes are made?"¹¹

World Wide Trends in Abortion¹¹

In the Scandinavian countries the abortion laws have been liberalized for some time. Recent statistics reveal the following information:

Incidence of Abortion

Country	Year 1940	Year 1956	Total Increase
Denmark	0.7%	6.0%	9 fold
Sweden	0.5%	3.5%	7 fold

Number of Abortions Per Year

Sweden	Rate/1,000 live births (1957-60)	3,000	27-32
Denmark		4,000	49-54

Switzerland recently reported that one therapeutic abortion is done for every 15 live births.¹¹

Japan in 1949 reported 2.69 million births and the abortion rate was 91/1,000 live births.

Year	Abortion Rate/1,000 Live Births
1949	91
1957	716
1961	653

Total live births decreased to 1.56 million. Total abortions done in last 15 years: 20,000,000.

In *Poland*, a recent paper reported on 561,000 abortions done with a mortality rate of 1/40,000 pregnancies and a very low morbidity rate.¹² When the opponents of abortion speak about the grave risks to which pregnant women are exposed at the time of a therapeutic abortion they ought to remember that in 1963 alone, 975 patients were admitted to the New York Metropolitan Hospital with serious complications arising from septic, criminal abortions.¹³ In Poland legal abortions are being done at the rate of 700,000 per year.¹³

In our hemisphere, *Chile* reports one abor-

tion done for every live birth, an increase from 1950-1954 when of every 100 women admitted for delivery in a hospital, 85 were admitted for abortions.¹¹ At one time in Chile 40% of all of Chile's hospital beds were filled with women who had infections as a direct result of criminal interference with pregnancy. In Uruguay there are two to three abortions for every live birth.¹³

Great Britain is at the present time almost certain to pass an "Abortive Bill" very similar in content to the recommendations of the American Law Institute.¹⁴ It has been estimated that £175,000 worth of National Health Service bedspace each month is occupied by septic abortion cases. In a London hospital, for every patient admitted for a therapeutic abortion, 50 are admitted as a result of criminal abortion.

Definition of the Problem in the United States

Criminal Abortion

In the United States alone it has been estimated that between 1,000,000 and 1,500,000 criminal abortions are done yearly.^{4,18} The number of deaths due to such abortions per 10,000 live births has doubled in the last 20 years from 1.6 to 3.1.¹⁶ It is known that between 5,000 and 10,000 women die each year in the United States from infections and injuries accompanying criminal abortions.^{4,15} Each day an average of 10 patients suffering from the effects of illegal abortions are seen at the Los Angeles County Hospital. Abortion is the single, largest cause of maternal death in California. While deaths from other causes have markedly declined, the death rate from abortion has remained static. The absolute number of deaths from abortion has doubled.¹⁷ The reduction of deaths from illegal abortions presents the greatest opportunity for reducing the over-all maternal mortality rate.

When one considers that not many more women die each year in this country from cervical cancer it becomes apparent that the deaths from illegal abortion are a major public health problem. It becomes perfectly obvious that physicians are willing to forget these women in favor of spending large sums

of money for such worthwhile projects as cancer detection, diabetes detection and tuberculosis detection and control. These women are forgotten because many people still think of desperate women with unwanted pregnancies, married or single, as promiscuous and demand that they be punished by society for their "wrongful" acts.

Therapeutic Abortion for Rubella

Total number of therapeutic abortions in U. S./year: 8,000-10,000.

In 1964, an epidemic year for rubella, in Buffalo, New York, rubella accounted for 36% of the indications for the therapeutic abortions done. About 20,000 malformed babies were born as a result of that epidemic or roughly 4-5 times as many as in the recent Thalidomide disaster. One wonders what it takes to shock people.¹⁵

It is stated that the over-all incidence of therapeutic abortion in the United States is one in 400-500 deliveries.

Place	Year	Number of Births or Deliveries ¹	Incidence
California	1952-56	224,823 deliveries	1/418
N.E. U. S. A.	1959	44,439 live births	1/463
N. Y. City	1960-62	499,927 live births	1/555
61 U. S. Hosp.	1963	522,578 deliveries	1/503

The over-all therapeutic abortion rate¹ in the United States is falling.

Place	Year	Ratio of Abortion/Births or Deliveries	
N. Y. City	1943-47	1/196 live births	} decrease of 65% in 20 yrs.
	1951	1/344	
	1960-62	1/555	
Mayo Clinic	1945-49	1/173 deliveries	
	1950-54	1/292	
Univ. of Virginia	1941-45	1/85 deliveries	
	1946-50	1/119	
	1951-52	1/337	
Sloane Hosp. for Women, Columbia U.	1950-55	1/69 deliveries	
	1956-60	1/225	

In New York City alone, the decline is about the same, in the range of 65%. During the years 1951-1962 the over-all frequency of therapeutic abortion in New York City declined by 50%.¹⁶

Year	Number of Therapeutic Abortions	Ratio/1,000 Live Births
1943-47	3,592	5.1
1949	668	4.3
1951-53	1,698	3.5
1954-56	1,096	2.2
1957-59	1,034	2.1
1960-62	875	1.8

Although the over-all frequency of therapeutic abortion has markedly declined, the "double standard" spoken of by Professor Eastman has become more apparent. The disparity between ethnic groups and socioeconomic levels on the one hand and the availability of therapeutic abortion has in fact widened.¹⁶ For example:

Sloane Hospital, New York City ⁷	
Ratio of private/ward patient: 4:1	
60 U. S. Hospitals, 1963	
Ratio of therapeutic abortions/live births: ⁷	
Proprietary Hospitals: 1/256	
Private service voluntary hospitals: 1/416	
Ward service voluntary hospitals: 1/1,429	
Municipal Hospitals: 1/10,000	
Obstetrical Cooperative (11 Eastern Hospitals), ¹⁹	
Therapeutic abortion rate: White patients 2.9/1,000 live births	
Colored patients 1/13,000 live births	
Sloane Hospital, New York City ⁸	
Private patients 1/55 deliveries	
Ward patients 1/224 deliveries	
Type of Institution	Frequency
Proprietary hospital	6.3/1,000 live births
Private service, vol. hosp.	3.6/1,000 live births
Ward service, vol. hosp.	1.9/1,000 live births
Municipal hospital	1.2/1,000 live births

Therapeutic abortion among white patients is more than five times as common as among non-whites and twenty-six times as common as among Puerto-Ricans.¹⁸ It becomes perfectly obvious that the affluent woman is much more likely to be aborted than her indigent sister. There is a downward trend in all therapeutic abortions, but it is greatest among Puerto-Ricans, less among non-whites and least among whites. About 90% of all the therapeutic abortions performed are done on white women.¹⁶ When considering deaths from criminal abortions, however, the converse is true.

Deaths From Criminal Abortions		
Race	10,000 Live Births 1945-65	
White	0.6 to 1.0	
Non-white	6.1 to 8.0	
Puerto-Rican	4.0 to 4.7	

It is seen, therefore, that as a result of denying therapeutic abortion to certain races

many more women die each year from the effects of criminal abortion. Not only is affluence a factor in being able to procure an abortion legally, but race and nationality play a significant role as well. We need, therefore, to equalize the opportunities for therapeutic abortion regardless of socioeconomic status, race, nationality and hospital service.

When one examines these inequalities in terms of the type of patient admitted to a particular hospital and the indications for abortion, the following is evident:¹⁶

Therapeutic Abortion, By Indication And By Type Of Care
N. Y. C. 1954-62

Indication	Prop. Hosp.	Pvt. Serv.	Ward Serv.	Municip. Hosp.
All indications	41.06	25.5	7.4	2.4
Mental disorders	26.0	14.3	2.6	0.9
Rheum. heart dis.	2.0	1.0	0.8	0.1
Other circ. disorders	1.2	0.8	0.3	0.1
Tuberculosis	1.4	0.6	1.4	0.2
Rubella	2.9	2.8	0.1	0.2
Malig. neoplasms	0.8	1.2	0.4	0.3
Benign neoplasms	0.8	0.4	0.2	0.1
Hypert. and toxemia	1.6	0.8	0.4	0.2
Diabetes	0.2	0.2	—	0.1
Renal disease	1.5	0.6	0.5	—
Nonspecific dis.	0.2	0.3	—	0.1
C.N.S. disorders	1.0	0.6	0.5	0.1
Rh incomp.	0.3	0.7	—	—
Others not stated	1.6	1.2	—	—

Therapeutic Abortion for Mental Disorders

It is interesting to note that mental disorders account for $\frac{2}{3}$ of the abortions done in proprietary hospitals, more than $\frac{1}{2}$ in the private services of voluntary hospitals and only $\frac{1}{3}$ in the ward services of voluntary and municipal hospitals. Ten times as many private patients have abortions done for psychiatric indications than clinic patients at Sloane Hospital for Women in New York City.¹ It is also well known that sterilization accompanies therapeutic abortion more than twice as often on the ward service whether the indication is medical or psychiatric.¹ Prior to 1950, psychiatric indications accounted for less than 20% of the therapeutic abortions done and since 1950, for 25 to 45%. This is an absolute as well as a proportionate increase. In New York City the number of therapeutic abortions over the last 10 years has declined steadily, but the per cent of therapeutic abortions done on psychiatric in-

dications has remained static, about 50%.²²

Psychiatric indications are given for nearly 94% of abortions done on unmarried women but for only 50% on married ones. The psychiatric criterion applies much more often to patients under 20 years of age and to those older than 39 years than to those in between.^{15,18} This correlates perfectly with the observation that abortion is most common early and late in the reproductive cycle of women. It seems that abortions for psychiatric reasons are almost exclusively the luxury of the rich. Abortion and psychiatric consultation are less common among the poor because they cannot afford them, they cannot find them, they are unaware of their benefits and they are less often referred for them by other physicians.¹

Contrary to general opinion, illegal abortion is more often a problem in the married woman with several children and less a problem in the single girl. The more children a woman has the more likely she is to seek an abortion. A much higher rate of criminal abortion occurs at younger ages and again later in life.⁴ The higher the educational level the greater is the tendency to seek an abortion. Astounding is the statistic that well over 80% of all pregnancies are criminally aborted in the unmarried college graduate.⁴ In the 1940s, almost no woman under 20 years had a legal therapeutic abortion, while in the 1960s such girls made up 12% of the total group. The nulliparous groups of patients increased from 20 to 40% of the total group. In the 1940s fewer than 10% of the women were unmarried; 40% are now single, widowed or divorced.^{15,18}

Discussion

It is obviously not the intent of any body of law to punish women with the risk of death for having illegal abortions; but this is the result. The present laws are supposed to protect the prospective mother and her unborn infant, but because the laws are too restrictive they discourage rather than encourage what is considered to be good medical practice. These laws undoubtedly drive many desperate women into the hands of the unskilled abortionist, the very man we wish to

protect them against. These same restrictive laws make it a certainty that only women in favored economic circumstances are able to procure safe termination of pregnancy, while those less fortunate, through no fault of their own, are forced to submit to the abortionist.

From what has been presented it is clear that more than 90% of the therapeutic abortions done at a large metropolitan eastern hospital do not fall strictly into the statutory requirements to "preserve the life of the mother."¹ Thus we become hypocrites who preach one thing and practice another. No one is content with breaking or circumventing the law . . . it behooves us therefore to use our influence to change the law.

No one should delude himself into thinking that modification of our present laws will eliminate criminal abortion. As long as there are restrictions, desperate women will find illegal abortionists. This is no reason, however, to abandon all attempts to correct these evils.

Kummer states that the forces in our society opposing abortion are well known and most obvious. What is also obvious is that these same social forces have not accomplished their stated goals, namely, maintaining morality and preventing abortion, injury and death.⁴ Some people are of the opinion that abortion, under any circumstance, is against morality. Those holding this view have every right to do so and can regulate their conduct in accordance with their beliefs. They must not, however, be allowed to impose their view on others who do not share it. This type of morality is subject to sharp dispute. Our present law prevents all physicians from performing an occasional indicated therapeutic abortion. The revised law would make therapeutic abortion legal; those who are not opposed can do such an abortion in full view of the law while those opposed need never per-

form such an act if they consider it immoral.

To those who say that by therapeutically aborting women with psychiatric illness the physician may be guilty of destroying brilliant offspring, it seems much more likely that the chances are far greater that he would be preventing countless heartaches and anguish. Those women aborted because they do not wish to risk producing a child with congenital deformities can always become pregnant again and bear normal, healthy children. To those physicians who say that all women illegitimately pregnant want to be pregnant, or who say that there are no psychiatric indications for therapeutic abortion and that by aborting medically and psychiatrically-ill patients physicians will only produce more psychiatric illness, it has been shown that moderate to severe psychiatric sequelae of induced abortion are indeed rare.²⁰ There is, on the contrary, a substantial incidence of post-partum psychiatric illness which accounts for 2% of female admissions to mental hospitals. To those who say that pregnant psychiatric patients rarely commit suicide, it seems clear that by driving these women to illegal abortionists one is flirting with death as well. It is obvious that psychiatrists are not always able to distinguish those patients who will or will not commit suicide; therefore, mistakes will be made on both sides. Since it has been shown that psychiatric indications for abortion are the largest single indication, it is clear that this is a game being played by both the psychiatrist and the obstetrician.

Only good can come from public discussion of these issues. It should be repugnant to physicians and lawyers that this kind of a dual standard for affluent and poor, black and white, should continue. When one considers that 1 to 1.5 million women resort to criminal abortion in the United States per year it speaks rather poorly for our concern for the welfare of all of our citizens.

References

1. Hall, Robert E.: Therapeutic Abortion and Sterilization. To be published.
2. Minnesota Statutes Ann. Sec. 617.18 (1953).
3. Whalen, M. J.: Therapeutic Abortion: A Survey

of Existing Legislation, Law Department, A.M.A., 1965.

4-22 May be secured from the author or the reprints.

A ship in harbor is safe, but that is not what ships are built for. — J. A. Shedd

An Obstetrician's View*

of Therapeutic Abortion

ERICK Y. HAKANSON, M.D.**
St. Paul, Minnesota

DURING THE past 30 years the incidence of induced abortion in the civilized world has risen progressively, resulting in enormous loss of life and health.

I think it is relevant to inquire briefly into the experiences of other countries before we review the facts that are available in our own country.

Legal Abortion

Outside the United States

Scandinavian medical literature provides the most comprehensive and best documented source material regarding therapeutic abortion. Strictly defined, the humanitarian and eugenic indications are considered as well as medical ones. However, an abortion is strictly under independent medical control and is not considered easy to obtain. The abortion rate in Sweden, in recent years, is approximately 3/100 term deliveries. Swedish authorities are concerned with the increasing number of its citizens who have been traveling to eastern European countries to get abortions. It is extremely difficult for a foreigner to get an abortion in Scandinavia.

Abortion became available in Eastern Europe in 1955-1957 on request for broadly interpreted social indications. Figure 1 shows that the number of induced abortions increased significantly, and in the case of Hungary in 1959, the number of abortions actually exceeded the number of births. It should be pointed out here that comprehensive family planning programs are just getting started in these countries.

In *Switzerland* there are 60-70 induced abortions for every 100 births, and two thirds of the abortants are married; the vast majority are healthy upper middle class mothers with small families.¹ Seventy per

*Part of the Symposium on Therapeutic Abortion read at the meeting of the Minnesota Obstetrical and Gynecological Society, Rochester, April 23, 1966.

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cent of the abortions are performed for psychiatric reasons, many of the abortants coming from other Western European countries.

Abortion has a very long cultural tradition in *Japan*, but it was not made legal and put under medical control until 1949. In that year Japan reported 2.69 million live births and 91 induced abortions/1000 live births. In 1957 the abortion rate had increased to 716/1000 live births, while 1.56 million births were recorded. The birth rate fell from 34.2 to 17.4/1000 population during that time. Japanese authorities feel that the number of reported induced abortions represents 50-60 per cent of the actual total.²

*See page 17.

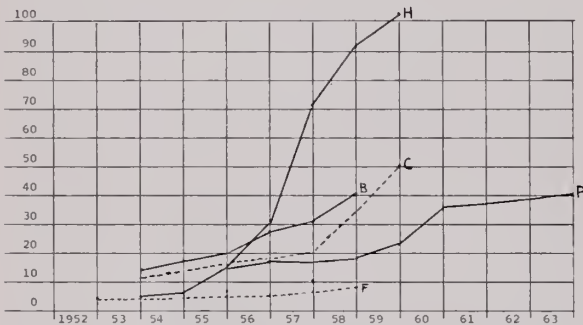


Fig. 1 — Number of Abortions per 100 Births (Bulgaria, Czechoslovakia, Finland, Hungary, Poland). **

**Lesinski, Jan: Abortion Indications and Procedures. P. 63, International Congress Series No. 102, Excerpta Medica Foundation, 1965.

FIGURE 2
Indications for Therapeutic Abortions in NYC†

Year	Rate Per 10,000 Live Births				%
	1951-53	1954-56	1957-59	1960-62	
All	34.8	22.2	20.6	17.5	-49.7
Mental disorders	12.1	11.3	11.8	10.6	-19.1
RHD	2.5	1.2	1.0	0.7	-72.0
Other circulatory diseases	1.3	0.6	0.6	0.6	-53.8
TB	3.3	1.4	0.9	0.3	-90.9
Rubella	1.2	2.0	2.0	1.2	0.0
Malignant neoplasms	1.0	0.6	0.9	0.9	-10.0
Benign neoplasms	3.0	0.6	0.3	0.2	-93.3
Hypertension and toxemia	2.8	0.7	0.8	0.6	-78.6
Nephritis and GU	1.3	0.7	0.6	0.6	-53.8
Diabetes	0.2	0.2	0.1	0.1	-50.0
Endocrine, nutritional	0.8	0.3	0.2	0.1	-87.5
Nervous system	1.0	0.9	0.3	0.3	-70.0
Rh incompatible	0.5	0.4	0.3	0.4	-20.0
Not stated	2.8	1.3	0.8	0.9	-67.9

†Gold, et al.: Amer J Pub Health 55:964, 1965.

We are all familiar with the large traffic in abortions in *Mexico and Puerto Rico*, a significant number, perhaps a majority, of these being performed on Americans.

Mortality

Hungary has reported a mortality rate for 1960-1962 of 5/100,000, more than half of the fatal abortions performed after the first trimester.³ Ninety-nine per cent of therapeutic abortions in Hungary are done during the first trimester. Scandinavian countries report a mortality rate of 64-68/100,000; but bear in mind that the indications are stricter, and, more importantly, therapeutic abortion can be carried out as late as 24 weeks. Approximately 25-35 per cent are done after the third month, and this group carries a disproportionate share of the mortality. Tietze quotes a mortality rate for therapeutic abortion in New York City for 1943-49 of 230/100,000.⁵ For comparison, the mortality rate for tonsillectomy in the United States is estimated at about 17/100,000 (1959).⁴

In the United States

Figure 2 illustrates that over the past twenty to twenty-five years there has been a steady decrease in the incidence of therapeutic abortion, and it reveals how the various indications have participated in the over-all decrease in therapeutic abortion. With the exception of mental disorders, rubella, malignant neoplasms, and perhaps Rh incompatibility, there has been a drastic reduction in the frequency of all medical indications.

Doctor Lyon* has amply demonstrated the *disparity in incidence* of therapeutic abortion between private and charity patients, and points out that the nonwhite is much less likely to get a therapeutic abortion than her white sister. On the other hand, deaths due to induced abortion in the poor nonwhite make up a majority of their maternal deaths.⁶

Gold et al. have shown that the incidence of abortion is directly *related to the age of the patient*, being significantly more common at the end of the reproductive career. This correlation is not influenced by parity.⁶

There is some evidence to indicate that the number of total induced abortions has an additional peak in the early years as well as in a better-educated, suburban white population sample.⁷

Briefly summarized, therapeutic abortion is *not routinely advocated for any category of disease*, but only after adequate workup can reasonably document that there exists a substantial risk to the individual patient's life or to her health.

From the results of the survey of metropolitan hospitals in Minnesota* one could conclude that therapeutic abortion is a rarity. More likely therapeutic abortion is more often performed than coded on the face sheet. My guess would be that less than 50 per cent of the total therapeutic abortions were specifically coded as such.

Indications

While there has been an impressive decrease in the number of therapeutic abortions in most categories, there has been an increase for so-called fetal indications,⁸ and a relative increase for psychiatric reasons. I think a fair estimate at the present time of the relative ratio of indications for therapeutic abortion in American hospitals would be:

Maternal medical disease	10-40%
Psychiatric indications	30-50%
Fetal indications	20-40%

Fetal Indications

Fetal indications include (1) rubella, (2) Rh incompatibility, and (3) serious inherited defects, plus other teratogenic influences. By far the vast majority of therapeutic abortions in this country for fetal reasons are those for rubella. Time does not permit a review of the many pitfalls associated with this important problem. The lack of easily available virological diagnostic techniques is certainly one of the most urgent problems at present. You have been told that the risk of embryopathy during the first trimester is somewhere in the vicinity of 10-20 per cent, and since many of these defects are not really so bad anyway (though I daresay they would be considered so by most of society), there is no reason whatever to

justify the interruption of pregnancy for this cause. I have no quarrel with that conclusion in view of the facts that were presented, but I do feel strongly that a very important principle of teratology has been neglected, viz., the fact that the results of the action of any deleterious effect, be it a virus, radiation, anoxia, high temperature, or drug, can be evaluated only in relation to the stage of the developing embryo at the time the noxious agent was active. Inasmuch as the first trimester represents a time period during which the zygote undergoes almost complete organogenesis and becomes a completely formed organism differing only in maturation from the second and third trimester fetus, any risk figure expressed as a percent of embryopathy for the entire period really has no meaning when applied to a specific individual problem.

Rubella-Induced Embryopathy

Our discussion with regard to rubella-induced embryopathy should be limited to those studies that fulfill the following conditions:

1. There should be prospective studies.

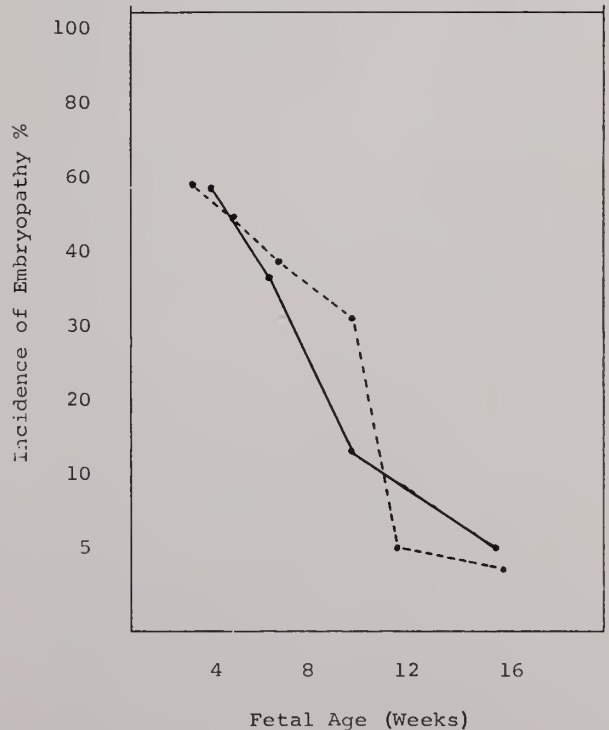


Fig. 3

--- Sallomi, S. J.: *Obstet Gynec* 27:252, 1966.
— Rendle-Short, J.: *Lancet* 2:373, 1964.

*See page 119.

2. Rubella should have been established by an M.D.

3. The date of the last menstrual period and active disease should be accurately known.

4. Infants must have been examined by a physician.

5. Only anomalies typical of rubella should be included: cataract, microphthalmus, congenital heart, microcephaly, deafness, and mental deficiency. Minor anomalies and such things as anencephaly and hydrocephalus were excluded.

6. No therapeutic abortions should have been done.

Rendle-Short⁹ and Sallomi¹⁰ have reported such carefully chosen studies, and they show remarkable agreement. The total anomaly rate for live-born babies exposed to rubella in the first trimester was 14.9 per cent. However, if the anomaly rates are plotted by week of gestation against a logarithmic scale of percent of embryopathy, we get an entirely different impression of the risk rate for rubella. We see that at two to four weeks the risk is probably in excess of 60 per cent and falls to about 30 per cent at six to eight weeks and to around 10 per cent at 10 weeks (Figure 3). Actually, we should refine this and plot the risk in relation to days of growth from 14 to 100 days after the last menstrual period.

The obstetrical outlook for women exposed to rubella is actually poor when expressed in terms of expected full-term live birth of a normal child. In the case of exposure of one to eight weeks, the average expectancy of a normal child at birth is 35.8 per cent.¹⁰ These figures are probably minimal, since they do not include the newer findings of *bone, spleen, and hematological abnormalities*, nor do they take into consideration that almost every long-term follow-up of these cases has revealed more cases of *hearing defects and specific learning difficulties and mental retardation* as these children enter school. In view of these risks I feel strongly that insofar as we know them, the facts ought to be available to the patients to the degree they are able to under-

stand them and that prospective parents themselves have a right to share in the decision for or against therapeutic abortion.

Psychiatric Indications

In regard to the controversy over psychiatric indications for abortion,¹¹ I think the main difficulty has been a confusion of terms. It seems obvious to me that Doctors Bernstein and Teeter* are talking about two quite different concepts. The orthodox view of trying to decide on narrowly-defined psychiatric grounds whether a given patient will commit suicide, for example, or if her reactive depression will relent, is, in my opinion, lateral to the main problem and will lead us only to a numbers controversy. As a matter of fact, it has been, I think, amply demonstrated that pregnant women carry a lesser risk of suicide. Also in Scandinavia, only about 5 to 8 per cent of the therapeutic abortions are performed for reactive depressions per se.¹¹ The real issue is this: after careful investigation of an individual's total life situation — past, present, and predictable future — are her, and to a lesser extent her family's and society's welfare and happiness best served by having her continue with the pregnancy or by her having an early and therefore safe interruption of it? It is inconceivable to me to try to make such a decision without taking into account *all* of the manifold and interrelated considerations which may relate to the stress of a given pregnancy.

Comments

Are we to believe that we can properly evaluate the effects of the stress of a pregnancy on a patient's health and happiness as though she existed in a vacuum? Are we to ignore her own feelings about the child, her ability to care for the child when born, the number of other children and the effects of the pregnancy on them, the stability of the husband and the marriage itself, the economic factors, and many other considerations too numerous to list? Some of you will undoubtedly object to the idea that socioeconomic considerations have a place in a decision vis-à-vis therapeutic abortion. We have witnessed in our lifetime the evolution of the concept that we cannot separate

*See pages 49 and 51.

"psyche" from "soma," and I think we all now accept it. But I think it is time now that we take the next step and recognize that we cannot separate the patient and his treatment from the multiplicity of factors in his heredity, environment, past experiences, and present situation. To wait for perfection of social welfare goals or the improvement of the human condition is, it seems to me, simply an excuse to avoid facing up to a very complex and difficult problem. Science seems to have condemned us to live in a world of rapid social change, and we must realize that it is no longer possible to operate according to absolute rules. We must adjust to meet new conditions in a world that we know will not become perfect in the predictable future.

We can all agree that the essential obligation of a physician is the health and welfare of his patient. As Peabody of Harvard said many years ago, the secret of the care of the patient is in caring for the patient. The treatment of disease should be impersonal; the care of the patient must be completely personal. Fletcher¹² has defined personalism as "that doctrine that correlates personality and value and holds that personality is a unique quality in every human being, and that it is both the highest good and the chief medium of our knowledge of good." Under the orthodox psychiatric view interruption of pregnancy for psychiatric reasons may never be justified, but under a personalistic frame of reference, such a conclusion is manifestly unwarranted. That contradiction, it seems to me is the crux of the controversy. Difficult as it may be, I think we have no choice but *must* grapple with this problem at all levels and with the help from experts in all fields until we get at least part of the truth.

Legally proven rape and incest are included under psychiatric indications. More properly these cases should be included under humanitarian indications. Many psychiatrists who are normally opposed to abortion for psychiatric reasons favor abortion in these circumstances. My own belief is that it is completely uncivilized to force such patients to go through a pregnancy.

However, the law does not recognize these indications, and every therapeutic abortion done for these reasons is illegal.

We must be frank in admitting that underlying philosophic or religious assumptions are probably the most important factor in influencing how we interpret the facts regarding abortion. Therefore, if you believe that a soul is infused at the time of conception, obviously such a belief, which is beyond rational argument, is hardly consistent with approval of abortion for any reason. On the other hand, there are many who feel that a fetus is not a moral or personal being since it lacks freedom, self-determination, rationality, and any ability to choose either means or ends; that it also lacks knowledge of its circumstances and therefore cannot rationally react to them; that quite obviously it has no social relationships. It may be said to possess a potential life, and indeed this fact is recognized legally; but to equate such a life in all respects with a living person is in my view a wholly unwarranted twisting of reality to fit preconceived theological assumptions. For one group to accuse another group of committing murder under these circumstances is not only grossly wrong but, in addition, serves merely to further confuse and compound the problem. Such questions are best left to the field of religion. I do not by this suggestion mean to imply that we can separate morals (as distinct from religion) from scientific questions. On the contrary, science, and especially medicine, which deals so intimately with the happiness of individuals and the good of society, must be concerned with morals. I simply deny the *exclusive* right of organized religion to determine the morals of medical practice for us.

We all recognize that therapeutic abortion may not be a "good" solution to what is a very complex socioeconomic, medical-moral problem. It is, I am convinced, in our present imperfect world, a necessary alternative for some unfortunate human beings. But regardless of the merits of this argument, I do not feel we should retain an archaic law that is widely disregarded by both the public and the medical profession. Furthermore, be-

cause the loss of life and health from illegal abortion is a very serious public health problem, I would urge the society to go on record as favoring the changes in our abortion laws as recommended by the American Institute of Law, but I would emphasize that, by itself, changing the law will not solve the problem. We need to do much more than take that necessary step. I would suggest the following additional steps:

1. We should go on record as advocating consultation centers for women seeking abortion, where specialized, intimate, non-punitive guidance can be given. Such centers, if they served no other purpose than providing badly needed statistics and long-term follow-up information, would fill a real vacuum in our knowledge.

2. We should go on record as approving sex and family-life education in our schools

from the earliest grades through college, with emphasis on the moral and social responsibilities of parenthood.

3. We should reiterate that contraception is an essential part of good medical care and make it easily available to everyone who wants it.

4. We should support research into all phases of human reproduction.

5. We should actively lobby for a voluntary sterilization act so that responsible parents in the older age groups who wish to permanently free themselves from the threat of additional pregnancies may do so.

I am advocating these five measures in the firm belief that in spite of our very serious difficulties we all want to work toward the same goal: the maximum conservation of human life and happiness.

References

1. Greenhill, J. P.: World Trends of Therapeutic Abortion and Sterilization. Clin Obstet Gynec

7:37, 1964.

2-12 May be secured from the author or the reprints.

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Courage is not the absence of fear; it is the mastery of it. — Christian Herald

Medical Indications for Therapeutic Abortion

An
Obstetrician's
View*

DAVID G. DECKER, M.D.**
Rochester, Minnesota

NO OBSTETRICIAN wants to be labelled an abortionist. Yet all of us, on occasion, are called upon to perform an abortion at the request of our colleagues. At such a time we look for scientific and ethical guidelines to help us make the right decision. Many hospitals and clinics have created "abortion committees" to help shoulder the responsibility and, depending upon their composition and rules of conduct, these committees may be of great help to the individual obstetrician.¹ But in the final analysis no committee can actually perform an abortion. This must be done by the individual practitioner. Only when we, as individuals, are sure of real benefit to the pregnant woman can we bring ourselves to interrupt the pregnancy. The literature on the subject is confusing and contradictory. It is often highly emotional and far from scientific. Controlled experiments are, at least to the present time, impossible.

So, in the majority of instances, the final decision is reached on the basis of (1) religion, (2) medical ethics, (3) current practice, (4) sympathy for, or empathy with, the patient, and (5) medical evidence. Most of us, strongly conditioned by our Judeo-Christian inheritance, find something repulsive in the act of abortion.² So also, all of us are conditioned by previous medical experience and teaching and, with the years, generally become rigidly opposed to, or vehemently in favor of, therapeutic abortion as an indicated procedure.

A review of the foreign literature from countries where a liberal attitude prevails does not help to solve the dilemma.³⁻⁶ Again, confusing and diametrically opposed views concerning the abortion program may emanate from the same country.

*Part of the Symposium on Therapeutic Abortion read at the meeting of the Minnesota Obstetrical and Gynecological Society, Rochester, April 23, 1966.

**Mayo Clinic and Mayo Foundation: Section of Obstetrics and Gynecology.

There are two questions involved: (1) are there any medical indications for therapeutic abortion; and (2) are there any psychiatric reasons for therapeutic abortion?

This discussion is directed to the first of these questions. Thirty years ago it was not so difficult to list medical indications for therapeutic abortion, but with rapid progress in the therapeutics of most diseases, it becomes increasingly difficult. For example, pulmonary tuberculosis, toxemia of pregnancy, hyperemesis gravidarum, hypertension, infectious nephropathy, thyrotoxicosis, diabetes mellitus, and acute rheumatic fever rarely appear as indications for abortion in series reported in the last 10 to 15 years.

In a review of the indications for therapeutic abortion at the Mayo Clinic in the past decade, certain broad categories have appeared as medical reasons for interrupting pregnancy.

Malignancy

Cervix

There is little question that treatment of an invasive carcinoma of the cervix results in the termination of pregnancy, and there is no argument at present regarding the necessity for that treatment—be it surgical or radiation therapy.

Pregnancy need not be interrupted for noninvasive carcinoma of the cervix when reasonable doubt about the diagnosis has been removed after conization.

Vulva

Pregnancy need not be interrupted as a part of the treatment of vulvar malignancy. Successful pregnancy can take place after radical surgery for this condition.

Carcinoma of the Breast

The indications for therapeutic abortion associated with carcinoma of the breast are tenuous. No statistical difference has been noted in the survival rate of patients who have aborted and those who have been allowed to proceed to term. The argument still rages as to whether nodal involvement should make the decision for abortion more definite.

The patient with an apparently estrogen-dependent breast cancer in whom metastatic lesions are being controlled by therapy should certainly be counselled against pregnancy and, if it occurs, may gain some months of life by having the pregnancy terminated. This would seem to be a relative indication for therapeutic abortion.

Also, the patient who has an inflammatory or rapidly progressing uncontrollable breast carcinoma would not seem a suitable candidate for pregnancy, but this is probably more a psychiatric than a medical indication for therapeutic abortion.

Malignancy of Bony Pelvis

Certain sarcomas of the bony pelvis that are treated by hind-quarter amputation may, in the pregnant patient, be treated more easily and with better healing if the pregnancy is terminated.

Carcinoma of the Rectum or Sigmoid

Primary treatment of malignancy in this region may result in the loss of the pregnancy but, depending on the location, this is not inevitable. The survival rate is affected by the pregnancy per se only when pregnancy interferes with adequate therapy.

Brain Tumors

Certain brain tumors become markedly edematous in association with pregnancy, and symptoms may increase out of proportion to the disease present. Also, vascularity is increased and surgery becomes more difficult technically. Therefore, in certain cases therapeutic abortion may be requested by the neurosurgeon and, in early pregnancy, probably should receive careful consideration.

Renal Disease

Chronic Renal Insufficiency

Such a condition, from whatever cause, may be a reason for therapeutic abortion. This is especially true where renal failure ensues and the patient is being maintained on the artificial kidney. The patient who is being considered for renal transplant usually will not become pregnant, but we are

now being faced with the post-transplant patient who should not become pregnant for six months to one year afterward. Prevention is obviously the better approach, but should pregnancy occur, consideration of interruption should be given.

Resistant Infection in Kidney

Rarely does resistant infection become severe enough in modern medical practice to indicate therapeutic abortion, but the rare instance, particularly with a solitary kidney, may arise when the urologist believes that the pregnancy is adversely affecting the control of the process.

Toxemia of Pregnancy

It is almost unheard of to consider abortion for toxemia, but in the rare case of early midtrimester fulminating toxemia with renal shutdown, interruption of the pregnancy may be lifesaving for the mother.

Cardiovascular Disease

Cardiac Surgery

The increasing scope of cardiac surgery has completely altered the indications for therapeutic abortion in congenital or acquired heart disease. At the present time no cardiac surgeon hesitates to operate on the pregnant patient. The only reluctance evidenced by cardiac surgeons at our institution was in a case in which the implantation of artificial valves required prolonged and intensive anticoagulation therapy.

Hypertension

With present modes of therapy, hypertension is rarely uncontrollable. Occasionally, however, severe pulmonary hypertension may still raise the question of therapeutic abortion.

Aneurysm

Surgical replacement of aneurysmal dilations is not a contraindication to pregnancy. Cerebral aneurysm with rupture may be a cause of acute episodes, but usually such patients are not particularly benefited by interruption of a pregnancy.

Diabetes Mellitus

Diabetic Nephropathy

The patient with severe diabetic nephropathy may be considered a candidate for interruption of pregnancy, but such nephropathy is no longer an absolute indication.

Diabetic Retinopathy

Severe diabetic retinopathy may be adversely affected by pregnancy and, particularly in those patients in whom pituitary-stalk section is contemplated, interruption of pregnancy may be requested.

Neurologic Disease

Rarely, a neurologic disease such as severe multiple sclerosis or myasthenia gravis may so compromise the health of the pregnant woman that the additional strain of pregnancy may seem unjustifiable to the neurologist. Again, this is a relative indication for abortion, and many factors must be balanced before a decision is reached.

Fetal Indications

Rubella

The reports on the incidence of congenital anomalies after rubella in the first six weeks of pregnancy are very confusing. Varied incidences of anomalies associated with the type of epidemic and the difficulty of diagnosis involved are evident. At present, wholesale therapeutic abortion for this condition does not seem valid.

Erythroblastosis Fetalis

The indications for abortion for this condition have been and are being altered by the techniques of exchange transfusion and more recently of intrauterine transfusion.

Inheritable Disease

At the present time, the problems of this broad group of conditions preclude any firm advice to the pregnant woman in most instances.

Conclusions

This list of conditions is not intended to be all-inclusive but rather is intended to indicate that there are few, if any, absolute

medical indications for therapeutic abortion in the present state of medicine. Almost all of the indications are relative. Of even more significance is the fact that each situation must be evaluated on its own merits. No blanket regulations are possible.

The obstetrician cannot lose sight of the fact that he is not only treating a patient in an immediate condition, but by performing a therapeutic abortion he may produce long-range effects that are both physical and mental. Therapeutic abortion is not an innocuous procedure. Chronic pelvic infections can be produced. Infertility or sterility may follow and, under the best controlled conditions, death may occur. Compounding the risk is not justifiable, and repeated abortion signifies failure of the obstetrician to control the situation. Where

therapeutic abortion is performed because of a chronic medical situation, sterilization should be done at the same time.

Recent studies from Denmark⁶ seem to emphasize that delayed guilt reactions may be a real problem and that some immediate psychiatric conditions may also be present. Improving the legal interpretation of therapeutic abortion is different from broadening the base for the procedure. Certainly that base, at least for medical indications, seems to be narrowing steadily.

In the final analysis, the obstetrician must make the ultimate decision whether or not to do a therapeutic abortion. He may be aided by consultation with his colleagues in various specialty fields and by the approval of his legal advisers; but in the operating room he stands alone.

References

1. McElin, T. W.: The Control of Therapeutic Abortion in a General Hospital. *Clin Obstet Gynec* 2:110, 1959.
2. Jeffcoate, T. N. A.: Indications for Therapeutic Abortion. *Brit Med J* 1:581, 1960.
3. Kolstad, Per: Therapeutic Abortion: A Clinical Study Based Upon 968 Cases From a Norwegian Hospital, 1940-1953. *Acta Obstet Gynec Scand* 36(suppl. 6):1, 1957.
4. Cee, K.: Zur klinischen Problematik der einzeiti-
- gen instrumentellen Schwangerschaftsunterbrechung. *Zbl Gynäk* 86:524, 1964.
5. Arén, Per: On Legal Abortion in Sweden: Tentative Evaluation of Justification of Frequency During Last Decade. *Acta Obstet Gynec Scand* 37(suppl. 1):1, 1958.
6. Berthelsen, Helge G., and Østergaard, Erling: Lethality and Incidence of Complications in Therapeutic Abortion in Denmark, 1953-1957. *Danish Med Bull* 6:110, 1959.

Oliver Wendel Holmes, M.D. To the Young Practitioner

We had a physician in our city whose smile was commonly reckoned as being worth five thousand dollars a year to him, in the days, too, of moderate incomes. You cannot put on such a smile as that any more than you can get sunshine without sun; there was a tranquil and kindly nature under it that irradiated the pleasant face it made one happier to meet on his daily rounds. But you can cultivate the disposition, and it will work its way through to the surface, — nay, more, — you can try to wear a quiet and encouraging look, and it will react on your disposition and make you like what you seem to be, or at least bring you nearer to its own likeness.

Male and Female

An opportunist is a man who, finding himself in hot water, decides that he needs a bath anyway.

An opportunist is a woman who finds the wolf at the door and appears later in a new fur coat.

— Watchman-Examiner

Democracy is liberty plus economic security. We Americans want to pray, think as we please — and eat regular. — Maury Maverick

The Importance of Corn Allergy

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WITH FEW EXCEPTIONS in the literature corn allergy has been minimized as shown by the following quotations. Hill¹: "Any food can cause asthma but not many foods commonly do so. Fish, egg, walnut, peanut, chocolate, are the most important." Unger²: "The only major foods which are frequent causes of migraine are chocolate, milk, wheat and pork." Carpenter³: "Foods are more likely to produce cerebral reactions than inhalants are. Thus, foods should be considered first. Milk, wheat, egg, chocolate, nuts, pork, and coffee are perhaps the most important." Withers and Hale⁴: "Although there is a difference of opinion regarding which foods most frequently cause symptoms [in food allergy], it is generally agreed that the foods used most often in the diet are usually the most common offenders. These are the basic ones, such as wheat, egg, milk, potato, beans, tomato, and chocolate." Davison⁵: "The ten most common foods incriminated [in cerebral allergy], in order of frequency, were: milk, chocolate, onion, cabbage, pork, eggs, fish and shellfish, tomatoes, nuts, and apples." Halpin⁶: "Since corn starch is practically free of protein, allergic reactions to its ingestion have been rare." Prickman⁷ and Coca⁸ found corn to be the least common. In a poll⁹ of allergists clinical symptoms from ingested corn were encountered in only 0.16% of 45,000 patients. This is in marked contrast to 16-30% of Rinkel, Randolph and others. Randolph¹⁰ found allergy to corn was present in 87, wheat in 85, milk in 75, and eggs in 67. The high incidence of corn sensitivity shown by these data makes it imperative that corn allergy be considered in all cases suspected of food sensitivity. Criepp¹¹ seems to agree with Randolph. Conrad¹² wrote an excellent guide on cooking in respect to milk, wheat, and eggs, but neglects corn. She recognizes that "corn syrup and corn sugars

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frequently cause trouble"; but in her "basic diet" (to avoid food allergens) she includes and allows the following foods, all of which may contain corn¹⁴: canned salmon, pork, bacon, ham, French dressing, potato chips. Brown and Brown¹³ in a discussion of gastrointestinal symptoms of food allergy include a case report of one patient who was skin-test sensitive to corn as well as to eleven other foods.

This conflict as to the importance of corn is probably due to (1) corn's ubiquity, the patient and the physician usually being unable to recognize corn when it is present (corn is found in over 130 everyday foods¹⁴); and (2) the lack of an adequate reliable diagnostic test for food allergy until the development of the provocative intradermal food test.¹⁵

In an attempt to resolve the contradictions in the literature regarding the importance of corn allergy, fifty consecutive patients were compared who reacted positively to one or more foods by the provocative intradermal food test. Of these fifty patients 38 were female and 12 male. Twenty females and five males gave a positive reaction to corn.

Symptoms of Corn Allergy

Numerous symptoms were elicited by these tests. Each symptom usually occurred in only one or two patients. This suggests that symptoms are hard to describe and are probably similar in several patients, each, however, expressing them differently.

The following symptoms which I interpreted as probably due to increased mucin production were described by various patients: throat feeling thicker, something in throat, formation of phlegm in throat, need of clearing throat, sinus drainage in throat, postnasal drip, runny nose, stuffy nose and throat, dry throat, dry mouth and nose, cough, frothy saliva.

Increased Capillary Permeability

These symptoms, interpreted as caused by increased capillary permeability, may well have been almost identical: full feeling in the upper chest, pressure in the chest similar to when patient had severe hives, stuffy chest, pressure in the middle of the head,

feeling of density in the head, feeling of exhilaration in the head, light-headedness, dizziness, bitemporal headache, frontal headache, occipital headache, retro-orbital headache, numbness of the throat and back of the head, tiredness, weakness, drowsiness, sleepiness, sweating, warm flush, eyes feeling puffed, burning eyes, trouble focusing, itching eye, itchiness all over, itchy face, roof of mouth itching, itchy throat, itchy nose, sneeze.

It is not clear whether any symptoms should be ascribed to smooth muscle contraction. Burping, which was noted in more than one patient, may not have been an allergic reaction. Most symptoms are ascribed to increased capillary permeability. Those few ascribed to increased mucin production may be secondary to increased capillary permeability.

The positive findings in the provocative intradermal food test in these 25 patients were confirmed by having them avoid corn in all its forms and note an alleviation of their symptoms, then having them deliberately eat corn in some form and note a recurrence of their symptoms. Various patients noted symptoms from various forms of corn in their food. The usual story was that they were able to associate their symptoms with all the forms of corn in their food only after studying a list of 130-odd foods which are known to contain corn.¹⁴ *In the illustrative case reports which follow, the foods containing corn are italicized for easier recognition.*

Case Reports

Case One

This 32-year-old woman had had wheezing and a stuffy nose since age 12, which required hospitalization for her asthma every year at odd times. She had noted that *ham* and *peanuts* caused wheezing. She had been avoiding eggs and milk because her local physician had found that these foods gave a positive skin test; nevertheless, avoiding milk and eggs had not helped her asthma. She had received some benefit from house-dust allergen injections. For several months she had had constipation followed by diarrhea, and spasms or cramps in her abdomen; proctoscopy and colon X rays were negative.

In eliciting details of her history, it was found that she often woke up at night with itchy, sandy eyes and swollen lids; during the day she gained five to seven pounds, with much burping and bloat-

ing, and in the evening abdominal distention forced her to loosen her clothing. These symptoms worsened about 45 minutes after her larger meals; often she would become very sleepy after meals, so that she was afraid to drive a car because of several near accidents due to dozing for a moment while driving.

She disliked bread but preferred dark to white bread (which is made from *bleached flour*). Her favorite foods were lettuce, *catsup* and *saucers made from catsup*, beef, liver, fish, and *corn*. *Corn* was the main vegetable in her home. Lettuce was eaten at almost every meal, sometimes even as a main dish such as a lettuce sandwich. She often craved lettuce, and usually put *salad dressing* or *mayonnaise* on it. Beans of any kind made her lips swell. She bloated from eating *popcorn* or *corn on the cob* or from drinking *beer*. Her favorite drink was *sloe gin sour*. She had found that *ham* or *peanuts* caused wheezing, and apples caused cramps in her abdomen. Her daily foods were *catsup*, *corn*, *corn flakes*, macaroni, potatoes, peas, lettuce, onions, Sanka, *corn meal*, *gelatin*, and beef. She had eaten a lettuce sandwich for supper the day before her office visit and recalled she could hardly stay awake after supper.

Provocative intradermal food test showed a positive reaction with corn (belching, formation of phlegm in her throat, and cough); with potato (sensation of swelling of the roof of her mouth and belching); and with lettuce (belching, yawning, and sleepiness). Egg and milk gave negative reactions.

After being on a corn-free diet she had no more bloating or erratic bowel habits; her asthma had improved tremendously, and she no longer gained several pounds of weight during the course of each day. The sandiness and itching of the eyes and the swelling of the eyelids also cleared, and she felt much

better in general. She broke her diet once by eating popcorn one evening and bloated so much that she had to change her clothes to accommodate the increase in girth, as had happened so often before going on her corn-free diet.

Case Two

Since early childhood this 14-year-old boy had had a chronic cough diagnosed repeatedly as bronchitis; once his chest X ray had shown pneumonia. For a long time he had also had a stuffy, runny nose, present year round, and worse at night when he lay down or when he was active or out in cold weather. Further complaints elicited on questioning were chronic tiredness, drowsiness after some meals, and enuresis until age 12. He had noted that eating *ice cream* gave him a headache, and *milk* "stuck to his throat" and tasted sour. His favorite foods were sour cream, hamburger, chicken, spaghetti, *cinnamon rolls*, *creamed corn*, *corn on the cob*, *corn bread*, *pies*, and *cookies*. He disliked liver, peas, boiled potatoes, chicken heart, baked beans, *milk*, *corn flakes*, *peanut butter*. The milk he drank came in *paper cartons*. The evening before testing for foods he had eaten hamburger sandwiches, *catsup*, and *corn chips*. His cough was worse that night. His lunch that day had consisted of *vegetable soup* and sandwiches of *peanut butter*, *tuna*, and butter. That afternoon he had felt very drowsy.

A swab of the material from the floor of his nasal cavity when stained revealed many eosinophils. Intradermal skin tests proved him to be sensitive to house dust. A provocative intradermal food test showed negative findings with wheat, but corn testing elicited the symptoms of drowsiness, definitely increased stuffiness of nose and throat, cough, itchy throat, and burping. These were cleared by a neu-

TABLE I

Corn product:	Equivalent corn-free product:
Bakery bread (made from bleached flour)	Frozen bread dough (made from unbleached flour)
Beer, whiskey, ale, cola	Rum, brandy, wine, vodka
Candy	Hershey's chocolate
Carbonated beverages	Cocoa, apple cider, Diet Pepsi-Cola
Catsup (commercial)	Homemade catsup
Cooking oil (e.g., Mazola)	Cottonseed oil, lard, olive oil, safflower oil
Corn flakes	Shredded wheat
Bleached flour	Rice flour, wholewheat cracked flour, rye flour, graham flour
Canned fruits, frozen fruits, fruit juices	Fresh fruits, water-packed fruits, unsweetened canned goods
Graham crackers	Rye-Krisp
Grape juice	Welch's grape juice
Gravy	Beef juice, butter
Ice cream	Dietetic ice cream
Commercial jams and jellies	Homemade preserves
Sausage, bologna, wieners	Fresh meats
Milk in paper cartons	Milk in glass bottles
Ready-to-bake mixes	Natural foods, raw foods home-cooked
Oleomargarine (from corn oil)	Butter, cottonseed oil oleomargarine, safflower oil oleomargarine
Peanut butter	Honey
Oil-packed salmon	Water-packed salmon
Restaurant salt	Pure salt
Powdered sugar	Crystal sugar
Syrup	Honey
Oil-packed tuna	Water-packed tuna
Canned vegetables sweetened	Unsweetened or water-packed canned vegetables
Distilled vinegar	Apple cider vinegar
Kosher foods	Passover foods

tralizing dose of corn. The test for milk produced a stuffy, sticky, sore sensation in the throat, which also cleared by injection of a neutralizing dose.

On desensitizing house dust injections and on a milk and corn-free diet he has become relatively asymptomatic for the first time in his memory.

Comments

Since thyroid insufficiency often occurs in allergy patients a survey was made in 1965 of the 100 pharmaceutical companies listed by the Red Book as manufacturers of thyroid tablets to see which brands did not contain corn, so that the allergy patient for whom thyroid was prescribed would not be receiving corn starch in his tablets. Of the 61 companies answering my letter of inquiry, only 16 did not use corn. The base or filler or binder used by these companies appeared to be lactose, talc, wood cellulose, mineral oil, cane or beet sugar, acacia, and/or potato starch. The most widely known of these 16 firms are Burroughs Wellcome & Co., Hynson, Westcott & Dunning, Wm. S. Merrell Co., and Warner-Chilcott Laboratories.

Other medications are also prone to contain corn. For the corn-allergy patient the safest procedure appears to be prescribing liquid medications other than syrups and the giving of injectables instead of oral medications where feasible.

Avoiding corn in the diet when there are about 130 foods containing corn and other corn contacts¹⁴ (including corn starch, corn syrup and corn oil) is a formidable task. The less determined patients and the less intelligent fail. Only one of my patients claimed she had no difficulty following the corn-free diet; she lived on a ranch where they did their own butchering, raised their own vegetables, did their own cooking and baking and canning, and "never" bought groceries in a store.

In order to give the corn-allergy patient advice more positive than a long list of foods to be avoided, a list of equivalents was prepared. Of course this list is not infallible and no list can be permanent, since

ingredients of commercial foods are always subject to change (See Table 1).

It has been theorized that since the neutralizing dose of food allergen removes the symptoms induced by the provocative dose in the provocative intradermal food test, then that same dosage and dilution should remove the symptoms caused by ingestion of that food. In my experience that is true. Selected patients have been given a bottle containing the neutralizing dilution of those foods to which they were allergic and disposable syringes and needles with instruction how to give themselves the neutralizing dosages as needed. In the dozens and hundreds of times these injections have been given the procedure has been almost 100% successful, according to the testimony of the patients.

Conclusion

1. Of 50 consecutive patients who had food allergies, 25 were allergic to corn, as demonstrated by the provocative intradermal food test and confirmed by a careful detailed history and by diet trials. Accordingly, corn should be considered one of the most important causes of food allergy.

2. In these patients there was a four to one preponderance of females.

3. Most drugs in tablet or capsule form are apt to contain corn.

4. Since corn is found in so many foods and is not easily detected in them, a list of corn-free foods should be given to the patient so that substitutions may be made. Such a list is presented.

5. A bottle containing the neutralizing dilution of corn and other allergenic foods may be given to the patient, who may self-administer the injection when the diet is broken and allergy symptoms result. In my experience this has been almost 100% successful in relieving allergy symptoms, according to the testimony of the patients themselves.

References

1. Hill, L. W.: Food Sensitivity in 100 Asthmatic Children. *New Engl J Med* 238:657, 1948.
2. Unger, A. H.: Allergy and Headaches. *Ann Allergy* 13:529, 1955.
3. Carpenter, R. C.: Inhalant Allergies with Headache as the Only Symptom. *J Lancet* 85:562, 1965.

4-15 May be secured from the author or the reprints.

Cerebral Blood Flow and Metabolism

During Experimental Hyperthermia (Fever)

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IT IS COMMON knowledge that high fever from any cause may be associated with delirium, stupor, coma and occasionally irreversible neurological deficit such as cerebellar ataxia. The neurologic and electroencephalographic disorders that result may be due to effects of hyperthermia on the enzymes or membranes of nerve cells, or on both. In children and occasionally adults, hemiplegia due to vascular occlusion may be precipitated by fever. The explanation for this has never been clarified. Possibly changes in clotting properties of the blood may occur, but if fever results in increased cerebral metabolism and blood flow, then regional neurological deficit may be expected to result in areas of diminished perfusion due to congenital anomaly or disease of cerebral vessels.

There are few observations of the electroencephalogram, cerebral circulation, and metabolism during hyperthermia; and those that are available do not agree. In order to clarify these problems, the following experiment was devised:

Changes in the electroencephalogram, cerebral blood flow, and oxidative metabolism were correlated during experimental hyperthermia in suitably anesthetized and immobilized monkeys and cats.

Method

Preparation of the Animals for Surgery

Sixteen *Macacus rhesus* monkeys of both sexes weighing 3 to 4 kg. and ten cats were used. Surgical anesthesia was induced by ether inhalation with atropine sulfate (0.2 mg/kg.) injected intravenously. The femoral artery and vein were cannulated and tracheostomy was performed. After surgery was completed, the incision sites were carefully anesthetized using 0.5% lidocaine hy-

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drochloride (Xylocaine®). Immobilization was achieved by intravenous injection of 20 mg. of gallamine triethiodide (Flaxedil®), and respiration was maintained with a Harvard Respirator. The maximum total dosage of gallamine was 40 to 60 mg.

Operative Exposure

Through a midcervical incision from the hyoid bone to the suprasternal notch, both carotid arteries and both internal jugular

*Model M-4001, Medicon Division of Statham Instruments, Inc., Los Angeles, California.

**Series 6000, Avionics Research Products Corp., Los Angeles, California.

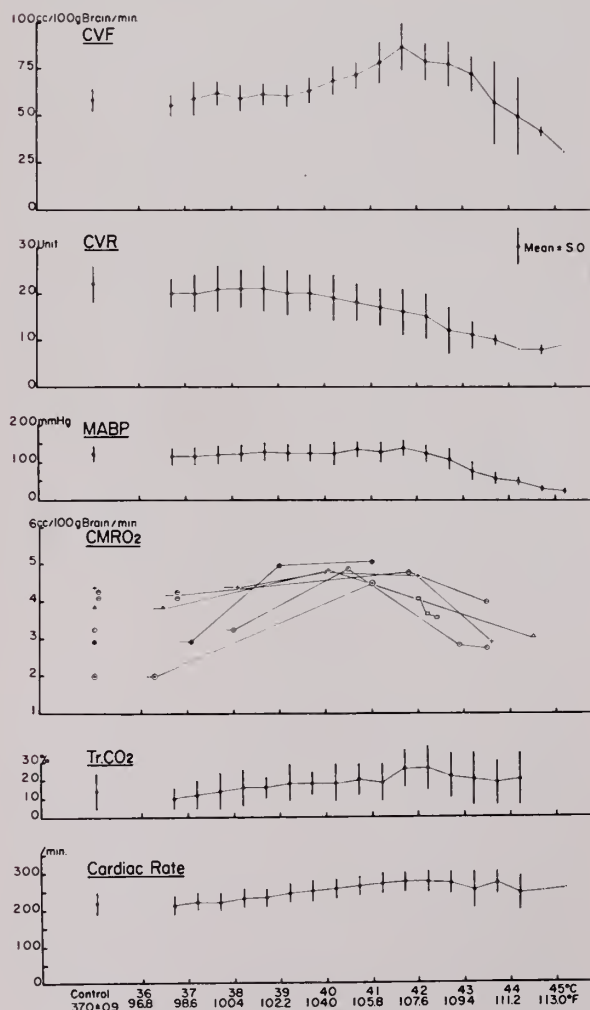


Fig. 1 — Summary of results of fever in the monkey. To show changes in cerebral venous flow, cerebral vascular resistance, mean arterial blood pressure, cerebral metabolic rate for oxygen, expired carbon dioxide from the trachea, and cardiac rate during induced hyperthermia in the monkey.

veins were exposed. When outflow from both internal jugular veins was measured (10 monkeys), the external jugular, vertebral and common facial veins and other tributaries of the internal jugular veins were ligated.¹ It has been shown that jugular venous outflow measured in this manner correlates in a statistically significant manner with cerebral blood flow measured by the nitrous oxide method.²

In the remaining six monkeys the internal carotid, external carotid, and vertebral flow were measured in various combinations. In three monkeys in which measurements of vertebral flow were performed, the left vertebral artery was exposed from its origin to the entrance into the foramen transversarium and the flow-probe was applied. The lower portion of the brachial plexus and the left stellate ganglion were sectioned to permit adequate exposure of the vertebral artery. The carotid sinuses were not denervated.

Determination of Blood Flow

Continuous determinations of blood flow were made with two Microflo sine-wave flowmeters* or one Microflo and one Metreflo square-wave flowmeters.

Because of technical difficulties in placing the flowmeter probe directly on the internal or external carotid artery, the remaining blood flow through the common carotid artery after ligation of the external carotid was named "internal carotid flow," and the remaining flow, after occlusion of the external carotid, was called "external carotid flow." It has been shown previously that this assumption is justified provided that the blood pressure does not fall to shock levels.³ In order to examine any possible differences between external and internal carotid flow, the flows were measured simultaneously in two animals, and the above assumption was found to be correct in the present preparation.

Induced Hyperthermia

Hyperthermia was induced by a warming pad irrigated with hot water. The rate of warming varied in each animal, but in most

of the studies the rectal temperature was raised from normothermic levels to 40-41.0° C. in two hours. Blood pressure was recorded with a Statham strain-gauge from a catheter threaded into the abdominal aorta via the femoral artery. Carbon dioxide concentration of the expired air was monitored with a Beckman Medical Gas Analyzer (Spinco Model LB-1). Recordings of blood pressure, blood flow and endotracheal carbon dioxide concentration were made by a Grass Model V Polygraph. Electroencephalogram and electrocardiogram were recorded with a Grass Model III-D Electroencephalograph. Rectal temperature was measured with a thermometer accurate to 0.1° C.

In the monkeys periodic samples of arterial and cerebral venous blood were drawn from the femoral artery and the internal jugular vein, and oxygen content was determined by the gasometric method of Van Slyke. In 10 cats, changes in the electroencephalogram and electrocardiogram, blood pressure and endotracheal carbon dioxide concentration were compared to observations in the monkey. In three cats, femoral artery flow was measured during hyperthermia. Since the changes in the parameters measured in the cat were the same as in the monkey, the results in the monkey will be described, and only those observations in the cats which are considered pertinent will be mentioned.

Results

The results of the experiments in the monkeys are summarized in Figure 1.

Arterial Pressure

Mean arterial pressure was calculated by adding one third of the pulse pressure to the diastolic pressure. In all monkeys mean arterial pressure was relatively high, varying from 87 to 145 mm. Hg., the average being 114 mm. Hg. (Standard deviation = ± 22.4) in the steady state. Changes in mean arterial pressure during hyperthermia are summarized in Figure 1.

In three monkeys hyperthermia was maintained around 41° C. In two of the remaining 13 monkeys in which hyperthermia was prolonged, mean arterial pressure remained

essentially unchanged until a rectal temperature of 41.5-42.4° C. was reached, when shock developed rapidly. In another two monkeys blood pressure decreased slightly but progressively, and at 41.5-42.9° C. circulatory collapse occurred. In eight monkeys mean arterial pressure first showed an increase, reaching a maximum at 41.5-42.9° C., blood pressure thereafter decreasing. In one experiment the blood pressure fell below 30 mm. Hg. when the temperature was only 40° C.

In mean arithmetic terms, mean arterial pressure increased gradually from 11 mm. Hg. (Standard deviation = ± 22.4) in the steady state to 138 mm. Hg. (Standard deviation = ± 18.9) at 41.5-41.9° C. (106.7-107.4° F.) and then failed rapidly (Figure 1).

Carbon Dioxide Content

Carbon dioxide content of the expired air

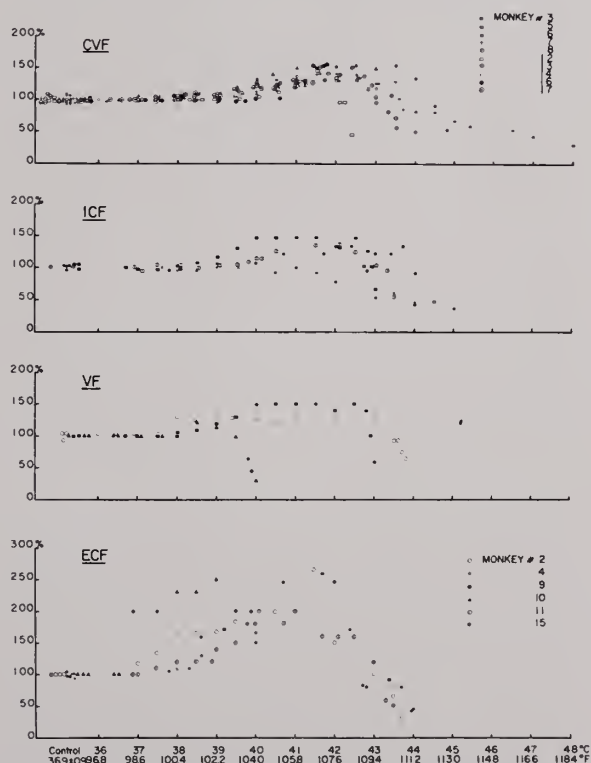


Fig. 2 — Summary of results of hyperthermia on blood flow through the major cephalic arteries in the monkey. To show changes in external carotid flow (ECF), internal carotid flow (ICF), and vertebral flow (VF) during hyperthermia in the monkey. Cerebral venous flow (CVF) also is shown for comparison.

increased steadily in all 16 monkeys except one in which the carbon dioxide content decreased briefly before the increase (Figure 1). Maximal values were obtained at 41.5-42.2° C. in nine of the 15 monkeys; thereafter the carbon dioxide content decreased. On the average, carbon dioxide increased from resting values of 2.0% (Standard deviation = ± 0.3) to a maximum of 2.8% (Standard deviation = ± 0.5) at 41.5-42.4° C. (106.7-108.3° F.).

In connection with the steady increase in tracheal carbon dioxide during hyperthermia, it should be pointed out that the animals were ventilated artificially at constant frequency and volume, so that the tachypnea usually seen in hyperthermia was prevented.

Heart Rate

Cardiac rate increased without exception. In eight of 13 animals in which hyperthermia was continued until shock, cardiac rate reached a maximum at 41.5-42.9° C. When average values were calculated for the group, the cardiac rate increased from 212 (Standard deviation = ± 28) in the steady state to 276 (Standard deviation = ± 03) at 42.0-42.4° C. (107.6-108.3° F.); thereafter it decreased.

Cerebral Blood Flow

Bilateral internal jugular venous flow was measured simultaneously in 10 monkeys; in seven of these, hyperthermia was continued until shock occurred, and in three a temperature of 41.0° C. (105.8° F.) was maintained for 60-80 minutes. In this series of 10 monkeys, cerebral blood flow, estimated in terms of cerebral venous outflow, ranged from 47.0 to 67.0 cc/100 g/Brain/min. in the steady state with a mean value of 57.7 cc. (Standard deviation = ± 6.5) at body temperature of 37.0° C. ± 0.9 .

During induction of hyperthermia, cerebral blood flow remained unchanged until body temperature reached 39.0-39.4° C. (102.2-102.9° F.). At this temperature mean cerebral venous outflow was 60.0 cc/100 g/Brain/min. (Standard deviation = ± 5.5 p > 0.1) when compared to the steady state (Figure 1). Above 39.4° C. cerebral venous

outflow increased steadily to reach maximal values of 86.0 cc/100 g/Brain/min. at 41.5-41.9° C. (106.7-107.4° F.) (p < 0.001). Above 41.9° C. cerebral venous outflow decreased rapidly.

Vascular Resistance

Cerebral Vascular Resistance ranged in the steady state from 1.7 to 2.6 mm. Hg/cc/100 g/Brain/min. for the seven monkeys in which warming was continued until shock developed, the average being 2.2 (Standard deviation = ± 0.4) at a temperature of 37.0° C. ± 0.9 . During induction of hyperthermia, cerebral venous outflow remained stable until 39.5-39.9° C. (103.1-103.8° F.); then it progressively decreased (Figure 1). The mean values at 39.5-39.9° C. and 40.0-40.4° C. were 2.0 (Standard deviation = ± 0.4) and 1.9 (Standard deviation = ± 0.5) respectively; but the decrease from the resting level of 2.2 was not statistically significant for either. At a temperature of 40.5-40.9° C. (104.9-105.6° F.) the decrease of cerebral vascular resistance to 1.8 (Standard deviation = ± 0.4) reached the level of statistical significance (p < 0.05).

Cerebral Metabolic Rate of Oxygen

This increased significantly during induction of hyperthermia. The control values for cerebral metabolic rate of oxygen in the steady state (36.3-38.1° C.) ranged from 2.0 to 4.4 cc/100 g/Brain/min., the average being 3.4 (Standard deviation = ± 0.8). During hyperthermia at body temperature of 40.0-42.0° C. cerebral metabolic rate for oxygen increased to 4.1-5.0 cc/100 g/Brain/min. with a mean of 4.6 (Standard deviation = ± 0.3). This increase of cerebral metabolic rate of oxygen from 3.4 to 4.6 (ca. 35% increase) was statistically significant (Figure 1). When body temperature exceeded 42° C. (107.6° F.), cerebral metabolic rate of oxygen rapidly decreased.

Regional Cephalic Blood Flow During Hyperthermia

Since quantitative blood flow through the internal carotid, external carotid, and vertebral arteries varied in the steady state in

different animals, measurements during hyperthermia were expressed as percentages of resting values (Figure 2). Values for internal jugular venous outflow are correlated for comparison.

Internal Carotid

General patterns to flow change in the internal carotid and vertebral arteries compared well with those in the internal jugular veins. In three out of four monkeys in which the *internal carotid flow* was measured, flow increases of 37-47% occurred during hyperthermia at 41-42.5° C. In one animal internal carotid flow did not increase during the course of experiment nor did any pressor response occur. At 42° C. the blood pressure and internal carotid flow decreased rapidly.

Vertebral Artery

Vertebral artery flow was measured in three monkeys, maximal increases being 31-50% at 40-43° C. Simultaneous flow measurements of both internal carotid and vertebral arteries in one monkey showed identical changes.

External Carotid

External carotid flow showed fluctuations related to those of blood pressure. At the beginning of the study external carotid flow and blood pressure records were a mirror image, i.e., sharp increases in blood pressure were accompanied by decreases in external carotid flow. During hyperthermia, this pattern was reversed, i.e., during sharp increases of blood pressure increases in flow followed.

Detailed mechanisms of this phenomenon are out of the scope of the present paper. However, it might be assumed that in the beginning, periodic vasoconstriction and the resultant increase in peripheral resistance are the main factors for paroxysmal increase in the blood pressure. When the body temperature was raised further and the peripheral vessels were dilated, any increase in the blood pressure, presumably of cardiac origin, produced passive distention of the peripheral vessels by higher pressure head, thus passively increasing the blood flow.

When there was any significant paroxys-

mal fluctuation of the blood pressure and blood flow, readings of the blood flow were taken at the lowest blood pressure levels. In all five studies where external carotid flow was measured there was an increase soon after hyperthermia was induced at a time when the internal carotid and vertebral flow still remained unchanged. The increase in external carotid flow was much greater than the increases of the internal carotid, vertebral, or internal jugular flow, maximal values appearing at 40-42° C. with a 100-160% increase. In one monkey flow measurements were not made beyond 38.6° C. because of technical problems with the flowmeter (Figure 2).

In three *cats* blood flow through the femoral artery was measured during hyperthermia. Femoral arterial flow, like external carotid flow, also started to increase after the onset of warming and rose to 360% of the steady state at 39.7-42.50 C.

In brief, internal carotid, vertebral artery, and internal jugular flow all showed maximum increases of 25 to 50% with one excep-

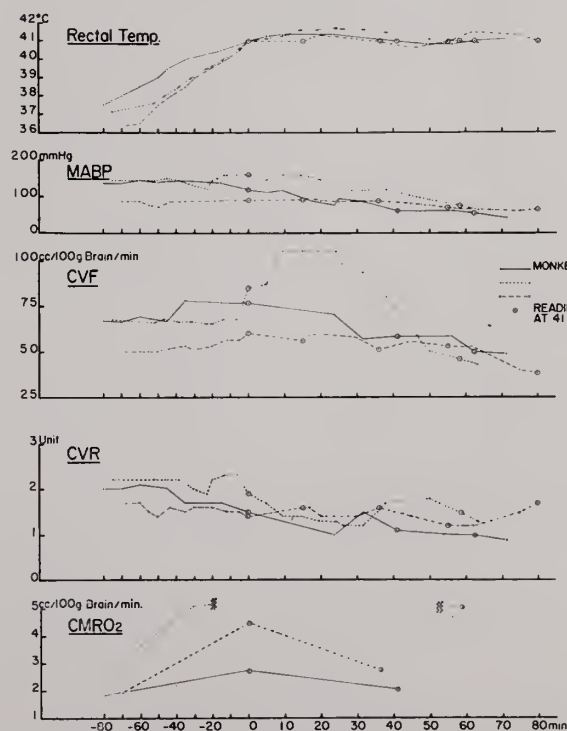


Fig. 3 — Summary of effects of sustained hyperthermia. To show the effects of sustained hyperthermia on mean arterial blood pressure, cerebral venous outflow, cerebral vascular resistance, and cerebral metabolic rate for oxygen in the monkey.

tion. Peripheral arterial flow, including the external carotid flow, increased at an earlier stage than cerebral blood flow, and maximum increases were greater.

Effects of Prolonged Hyperthermia

In three monkeys the temperature was maintained around 41.0° C. (105.8° F.) for 60-80 minutes; the results are summarized in Figure 3. In one monkey the temperature increased by 0.4° C. after warming was discontinued, then decreased to 41.0° C. approximately 40 minutes later. During this interval of 40 minutes, mean arterial pressure decreased from 120 mm. Hg. to 62 mm. Hg. Cerebral venous outflow increased from 65 cc/100 g/Brain/min. in the steady state to 77 cc. at 41.0° C.; but when the temperature decreased to 41.0° C. again, cerebral venous outflow fell to 58 cc., below the resting level. Cerebral vascular resistance progressively decreased during the 40-minute interval from 1.5 to 1.0 unit, and cerebral metabolic rate for oxygen decreased from 217 to 2.1 cc/100 g/Brain/min.

A similar progressive decrease in mean ar-

terial pressure, cerebral venous outflow, and cerebral vascular resistance was likewise observed during sustained hyperthermia in one monkey; in another the mean arterial pressure remained stable, but cerebral venous outflow and cerebral metabolic rate for oxygen decreased.

Electroencephalographic Changes During Hyperthermia

Unipolar and bipolar electroencephalograms were recorded in all animals except one cat. Except for periodic changes accompanied by paroxysmal elevations of blood pressure, the electroencephalogram remained normal until the temperature reached 41.0-42.0° C. (105.8-107.6° F.). When these temperature levels were exceeded, sporadic bursts of slow waves appeared in the theta range. In 12 monkeys the temperature was raised further and sporadic delta waves appeared at 42.0-43.4° C. (107.6-110.1° F.). Between 43.0-44.0° C. (109.4-111.2° F.) diffuse delta activity appeared, and the record became flat between 43.5-46.0° C. (110.3-114.8° F.).

In every case where correlation was possible, the increase of theta and appearance of delta waves coincided with the rapid decrease in cerebral blood flow (either jugular outflow or arterial inflow) from maximal to subnormal levels. In one monkey the electroencephalogram slowing appeared at the relatively low temperature of 39.5° C. and became flat at 40° C. This monkey's cerebral venous outflow also decreased prematurely at 39.8-39.9° C. along with the appearance of delta waves in the electroencephalogram.

During sustained hyperthermia at 41° C. the electroencephalogram showed progressive slowing despite a stable temperature of around 41° C.; this was also accompanied by a progressive decrease in cerebral blood flow and metabolism (Figure 4B). Seizure activity in the electroencephalogram was observed in three of 11 cats between 42-45.8° C.; but spike activity was not observed in the monkeys.

Discussion

Although hyperthermia is known to cause

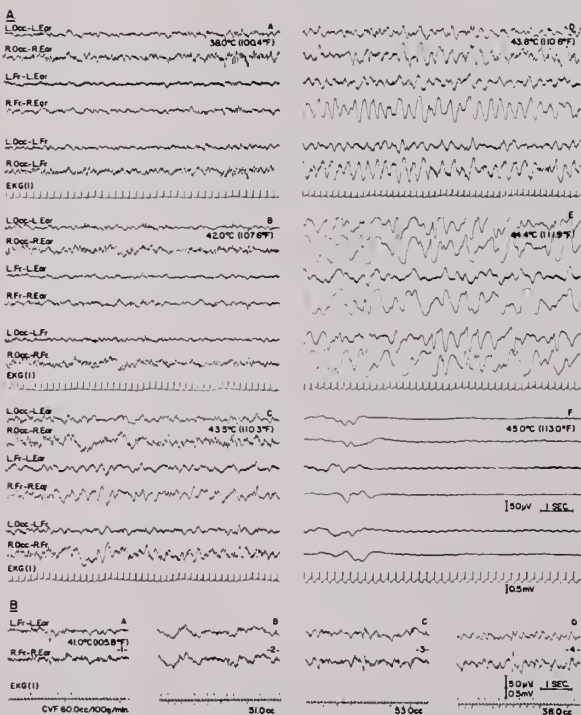


Fig. 4 — To show progressive electroencephalographic changes during induced hyperthermia in the monkey.

significant changes in circulation and metabolism of the body as a whole as well as of several organs,³ few measurements have been made of the effects of fever on cerebral blood flow and metabolism, and these few are not in agreement.

Increased Cerebral Oxygen Consumption during Fever

In-vitro studies of the rat brain showed increased oxygen consumption as the temperature reached 40° C. At 37.5° C. or below, QO_2 was constant for more than three hours; however, at 40° C. and above, QO_2 diminished the longer the temperature was sustained.⁴ Himwich et al.,^{5,6} using rat brain, noted increased cerebral oxygen uptake with increasing temperature between 25° C.-44° C. Above 44° C. the increase in oxygen uptake ceased. They also showed that above 40° C. sustained hyperthermia for 50 to 60 minutes resulted in a rapid reduction of oxygen uptake when compared with measurement at 20 minutes.

Despite the above results Dixon⁷ reported that the oxygen uptake of rabbit brain was only slightly higher at 42° C. than at 37° C.; at 45° C., however, oxygen uptake was increased by 100%.

Arteriovenous Oxygen Difference

Cerebral arteriovenous oxygen differences in man were reported to be increased by more than 2.0 vol. % during fever therapy. This was found in 11 of 15 subjects treated for general paresis, using typhoid vaccine, malaria, or external heat.^{8,10} It was concluded that during hyperthermia in man, either cerebral metabolism increased to a greater degree than in other parts of the body or cerebral blood flow decreased. Contrary to these findings, Looney and Borkovic⁹ reported essentially no change in cerebral arteriovenous oxygen differences in 12 paretic patients treated with diathermy.

Cerebral Blood Flow and Metabolism

To our knowledge the only measurements of cerebral blood flow and metabolism in man during fever therapy were reported by Heyman et al.⁸ They measured cerebral blood

flow and oxygen consumption by the nitrous oxide method during fever induced by typhoid pyrogen or malaria. In 13 patients with asymptomatic neurosyphilis, cerebral blood flow and cerebral metabolic rate for oxygen were normal in the afebrile state and showed minimum changes during fever up to 101-104° F. (38.3-40.0° C.). Fourteen subjects with paretic neurosyphilis, however, showed cerebral blood flow and cerebral metabolic rate of oxygen values which were abnormally low in the afebrile state but which increased on the average by 30% and 24% respectively during fever. Although cerebral blood flow remained unchanged in asymptomatic neurosyphilis, dilatation of cerebral vessels must have occurred, since cerebral blood flow remained unchanged despite significant decreases in blood pressure. Furthermore, in the group with general paresis, cerebral blood flow increased despite the decrease in blood pressure, which can only be attributed to cerebral vasodilatation.

In the present experiments, cerebral venous outflow remained essentially unchanged until a temperature of 39.0-39.4° C. was reached; then it increased steadily and significantly. Undoubtedly the increase in cerebral venous outflow was partly due to the rise of blood pressure. The progressive decrease in cerebral vascular resistance, however, indicated that the rise of blood pressure was not the major factor, but that considerable cerebral vasodilation occurred during induced fever, probably related in part to increased carbon dioxide production during fever, as evidenced by the increase in expired carbon dioxide levels.

Cerebral metabolic rate for oxygen increased significantly at 40-42° C. The increase was larger if values in the steady state were low, since values at 40.0-42.0° C. became uniform. The average increase in cerebral oxygen metabolism was 35% and correlated well with the average increased cerebral blood flow of 30-50%.

If the temperature was increased beyond 42° C., cerebral venous outflow and cerebral oxygen metabolism decreased rapidly and the electroencephalogram deteriorated. Under the conditions of these experiments the

critical body temperature for maintenance of cerebral circulation and function appeared to be around 42° C. (107.6° F.).

When hyperthermia (around 41° C. rectally) was maintained for 60-80 minutes, both cerebral blood flow and cerebral oxygen metabolism tended to decrease with progressive deterioration of the electroencephalogram. These results are in good agreement with *in-vitro* studies of the oxygen metabolism of the rat brain by Looney and Borkovic and by Himwich et al.,⁶ which also showed that both the level and the duration of hyperthermia were important in determining its effects on cerebral metabolism.

The results reported here are consonant with the conclusion that hyperthermia increases cerebral metabolism and blood flow between 39° C. and 41° C. Above this temperature cerebral metabolism and blood flow are reduced, presumably due to cerebral enzymatic damage.

Summary

1. Hyperthermia was induced by a heating-pad in immobilized, regionally anesthetized, artificially ventilated rhesus monkeys.
2. Cerebral blood flow remained un-

changed until rectal temperatures of 39.0-39.4° C. were reached. After this, cerebral blood flow increased steadily until a maximal increase of 30-50% was obtained at 41.5-41.9° C.

3. Cerebral oxygen consumption increased significantly during hyperthermia, the average increase in cerebral oxygen metabolism at 40-42° C. being 35% of the steady state.

4. Although the increase in cerebral blood flow and cerebral oxygen metabolism was significant, they appear to be relatively less than the large increases found in other organs and tissues.

5. Above 42° C. cerebral venous outflow and cerebral oxygen metabolism suddenly decreased and the EEG deteriorated progressively.

6. If body temperature was maintained at moderate levels of hyperthermia (ca. 41° C.), cerebral venous outflow and cerebral metabolic rate for oxygen progressively decreased and the EEG became progressively abnormal despite maintenance of constant temperature.

Acknowledgments

Mr. Peter Miller provided technical assistance.

References

1. Meyer, J. S., Ishikawa, S., and Lee, T. K.: Electromagnetic Measurement of Internal Jugular Venous Flow in the Monkey. Effect of Epilepsy and Other Procedures. *J Neurosurg* 21:524, 1964.
2. Meyer, J. S., Gotoh, F., Tomita, M., and Akiyama, M.: New Techniques for Recording Cerebral Blood Flow and Metabolism in Subjects with Cerebrovascular Disease. In *Cerebral Vascular Diseases, Fifth Princeton Conference*, Millikan, C., Siekert, R., and Whisnant, J., Editors. Grune and Stratton, New York, New York. In Press, 1966.
3. Symon, L., Ishikawa, S., Lavy, S., and Meyer, J. S.: Quantitative Measurement of Cephalic Blood Flow in the Monkey. A Study of Vascular Occlusion in the Neck Using Electromagnetic Flowmeters. *J Neurosurg* 20:208, 1963.
4. Field, J., Gohrman, F. A., and Martin, A. W.: Effect of Temperature on the Oxygen Consumption of Brain Tissue. *J Neurophysiol* 7:117, 1944.
5. Himwich, H. E., Bowman, K. M., Fazekas, J. H., and Goldfarb, W.: Temperature and Brain Metabolism. *Amer J Med Sci* 200:347, 1940.
6. Himwich, H. E., Bowman, K. M., Goldfarb, W., and Fazekas, J. H.: Cerebral Metabolism during Fever. *Science* 90:398, 1942.
7. Dixon, K. C.: The Effect of Rise in Temperature on the Carbohydrate Catabolism of Cerebral Cortex. *Biochem J* 30, pt 2:1483, 1936.
8. Heyman, A., Patterson, J. L., Jr., and Nichols, F. T., Jr.: The Effects of Induced Fever on Cerebral Functions in Neurosyphilis. *J Clin Invest* 29:1335, 1950.
9. Looney, J. M., and Borkovic, E. J.: The Changes Produced on the Oxygen and Carbon Dioxide Content of Arterial and Venous Blood of the Brain during Diathermy Therapy for General Paresis. *Amer J Physiol* 93:177, 1942.
10. Altschule, M. D., Freedberg, A. G., and McManus, A. G.: Circulation and Respiration during an Episode of Chill and Fever in Man. *J Clin Invest* 24:878, 1945.

The art of living consists in keeping earthly step to heavenly music. — Panin

It's the Law

A SUMMARY OF EXISTING LEGISLATION IN REGARD TO THERAPEUTIC ABORTION IN THE UNITED STATES.

PREPARED FOR THE MINNESOTA OBSTETRICAL AND GYNECOLOGICAL SOCIETY MEMBERS, ROCHESTER, MINNESOTA, APRIL 23, 1966.

A therapeutic abortion is an abortion performed out of necessity. All of the states have criminal statutes dealing out severe penalties for criminal abortion, but, with one or two exceptions, each state has recognized necessity as justification.¹

The majority of the states, 41 to be exact, agree that an abortion is allowable if it is performed "to save the life of the mother." Twenty-five of these states flatly exempt from criminal liability the situation where an abortion is necessary to save the mother's life.²

Nine states: Connecticut, MINNESOTA, Missouri, New York, South Carolina, Virginia, Washington, West Virginia and Nevada carry their statutes a step further and exempt abortions necessary to "save the life of the mother or her child."³

Eight states: Florida, Georgia, Kansas, Mississippi, Wisconsin, Nebraska, New Hampshire and Ohio neglect to mention the child, yet are liberal enough to negate any notion of criminal liability per se.⁴

Two states stand out among the rest for their lack of exception. Louisiana flatly recites a statute making all abortions criminal. The Louisiana Medical Practice Act does, however, set forth the grounds upon which a doctor's license may be revoked, and this includes "any abortion unless it is done for the relief of a woman whose life appears in peril after due consultation with another physician." This does not express authorization but it does suppose that this reasoning could be construed as permissive.^{5,6}

Pennsylvania is the other state notable for its conservative stand. This state does, however, qualify the crime of abortion with the word "unlawful," thereby impliedly recognizing the possibility of a lawful abortion.⁷ There have been no Pennsylvania cases which have defined this term in relation to the statute.

Seven jurisdictions: Alabama, Colorado, District of Columbia, Maryland, Massachusetts, New Jersey and New Mexico,⁸ and also the Model Penal Code of the American Law Institute either definitely or apparently take the liberal viewpoint that necessity grave enough to warrant therapeutic abortion lies in the danger to the HEALTH of the mother.

Specifically, the jurisdictions state:

Alabama: . . . "unless the same is necessary to preserve her life and health and done for that purpose. . . ."

Colorado: . . . "unless it is done to save the life of the woman or to prevent serious and permanent bodily injury to her."

District of Columbia: . . . "unless the same was done as necessary for the preservation of the mother's life or health."

Maryland: . . . "providing that no other method will secure the safety of the mother."

Massachusetts: . . . "unlawfully." The Court held that "if a physician in good faith believes the abortion to be necessary to prevent serious impairment of a patient's mental or physical health, the abortion is considered justified."

New Jersey: . . . "without lawful justification." The Court held that the statute was designed" . . . not only for the protection of the unborn child, but to protect the life and health of the mother as well."

New Mexico: . . . "an abortion may be lawfully permitted to preserve the life of the woman or to prevent serious and permanent bodily injury."

State of Minnesota Statute:⁹

Every person, who with intent thereby to produce the miscarriage of a woman, unless the same is necessary to preserve her life, or that of the child with which she is pregnant, shall (1) prescribe, supply, or administer to any woman, whether pregnant or not, or advise or cause her to take, any medicine, drug, or substance; or (2) use, or cause to be used, any instrument or other means, shall be guilty of abortion and punished by imprisonment in the state prison for not more than four years or in a county jail for not more than one year.

Whoever shall manufacture, give, or sell an instrument, drug or medicine, or any other substance, with intent that the same may be unlawfully used in producing the miscarriage of a woman, shall be guilty of a felony.

A pregnant woman who takes any medicine, drug, or substance, or uses or submits to the use of any instrument or other means with intent thereby to produce her own miscarriage, unless the same is necessary to preserve her life, or that of the child whereof she is pregnant, shall be punished by imprisonment in the state prison for not less than one year nor more than four years.

Recommended or Proposed Minnesota Criminal Code 1963:*

A therapeutic abortion is justified (a) if performed by a licensed physician, (b) if performed in a licensed hospital and (c) any of the following conditions exist: (1) rape, (2) necessary to save the life of the mother or avoid grave impairment of the physical and mental condition of the mother or to prevent birth of a child with grave physical or mental defects and (d) if approved by two other physicians.

Recommendation of the American Law Institute in its Model Penal Code of 1959:

"A licensed physician is justified in terminating a pregnancy if (a) he believes that there is substantial risk that continuance of the pregnancy would gravely impair the physical or mental health of the mother or that the child would be born with a grave physical or mental defect, or the pregnancy resulted from rape . . . or from incest and (b) two physicians, one of whom may be the person performing the abortion, have certified in writing their belief in the justifying circumstances, and have filed such certificates prior to the abortion in the licensed hospital where it was to be performed or in such other place as may be designated by law."

In 1953, a judge in Oregon declared "that the interpretation by physicians of what is good for a woman's health takes precedence over any restrictions that are imposed by criminal law."¹⁰

There has never been a single case reported of a conviction of a physician for the performance of an abortion if the abortion was done in a licensed hospital.^{11,12,13}

In no state is potential deformity of the fetus an acceptable excuse for abortion.^{1,12}

*The above proposal was defeated in Committee and did not reach the Legislature for a vote.

IT'S THE LAW

Laws Differ from State to State

State	1	2	3	4	5	6	7	8	9	10
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Alabama						•				
Alaska	•									
Arizona		•								
Arkansas		•								
California	•									
Colorado					•					
Connecticut			•							
Delaware	•									
Dist. of Columbia						•				
Florida	•									
Georgia	•									
Hawaii		•								
Idaho	•									
Illinois	•									
Indiana	•									
Iowa		•								
Kansas	•									
Kentucky	•									
Louisiana										•
Maine	•									
Maryland							•			
Massachusetts								•		
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Minnesota			•							
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South Carolina			•							
South Dakota	•									
Tennessee	•									
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Utah	•									
Vermont	•									
Virginia				•						
Washington			•							
West Virginia				•						
Wisconsin		•								
Wyoming	•									

- 1 — to preserve the life of the mother
- 2 — to save the life of the mother
- 3 — to preserve the life of the mother or that of her child
- 4 — to save the life of the mother or that of her child
- 5 — to preserve the mother's life or prevent serious bodily injury

- 6 — to preserve the life or health of the mother
- 7 — to secure the safety of the mother
- 8 — willful or unlawful abortion a crime, without specific exception
- 9 — any abortion that is malicious or without justification a crime
- 10 — no exception to crime of abortion set forth in statute

References may be secured from Fred A. Lyon, M.D., 127 South Tenth Street, Minneapolis.

PRESIDENT'S LETTER

President's Letter Continued from Page 9

we are really trying to make this a very worthwhile postgraduate meeting for each of you, regardless of your specialty. The entire program attempts to cut across as many fields as possible.

There will be no banquet on Monday this year. Rather than plan anything else, we thought that you might like to have a free evening for a change, to get together with old friends, have a whing-ding, or both!!!

In view of the current battle now being

waged in the California courts by the physicians of that state, who believe their abortion laws to be antiquated, I should be remiss if I did not call to your attention numerous viewpoints on that subject expressed in this issue of your journal.



C. G. Sheppard, M.D.
President
Minnesota State Medical Association

Legislation Voted Upon by Minnesota Obstetrical-Gynecological Society*

State of Minnesota Statute

Every person, who with intent thereby to produce the miscarriage of a woman, unless the same is necessary to preserve her life, or that of the child with which she is pregnant, shall (1) prescribe, supply, or administer to any woman, whether pregnant or not, or advise or cause her to take, any medicine, drug, or substance; or (2) use, or cause to be used, any instrument or other means, shall be guilty of abortion and punished by imprisonment in the state prison for not more than four years or in a county jail for not more than one year.

Whoever shall manufacture, give, or sell an instrument, drug or medicine, or any other substance, with intent that the same may be unlawfully used in producing the miscarriage of a woman, shall be guilty of a felony.

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*See page 136.



Editorials

Psychiatric Indications for Abortion*

Pro

ABORTION IS one of the most emotionally charged subjects upon which I have ever had to write.

We can say that there are very few indications for abortion; we can say there are no indications for abortion. To turn our back on the problems by pronouncing that there shall be no abortions, that there are little or no medical indications for abortion, is, to me, an absurdity of astounding proportions. And yet, for the most part, our laws and a considerable number of our professionals seem to insist that this be the case. Such insistence is the denial of certain natural laws, a denial of certain inalienable truths, and such denial does not behoove the man of science. The voice of the people may well resolve the problem, and those of us who get mired in the arguments may well awaken to find the matter resolved by others, much to our consternation and perhaps relief.

An understandable but deplorable dilemma in this whole situation is the stand we medical men take; all too rarely do we ask others outside the profession to help us. The dilemma is seen in the position we take when we ask: 1. What are the psychiatric indications for an abortion? 2. What are the medical indications for an abortion? 3. Can you prove that an abortion will

save this mother's life? 4. Can you prove that an abortion will not damage the health of the mother, i.e., lead to depression, sterility, or frigidity?

What I am trying to get at is that our framework for making decisions appears to be too narrow. This narrow framework is what has made us decide at certain times that all schizophrenic women should be aborted or sterilized. It is easy to find schizophrenic symptomatology, but I don't know if any studies indicate that even a majority of the schizophrenic women make bad mothers or reject their infants.

A very deplorable thing adding to the polarization of opinions into sharply defined pros and cons is the secretive nature under which our evaluations, our operations and our conferences have to take place. In doing so, we would appear to be involving ourselves in both a social and psychological injustice.

Statistics of various sorts have found, over the past 80 years, that one condition after another has been at the head of the list as an indication for abortion. Claims have been made that medical reasons have been used to justify abortions when socio-economic pressures were the real reason. I believe this is true.

If medicine has been used to justify the many abortions motivated mainly by socio-economic pressures, then Dr. Joseph Ryan**

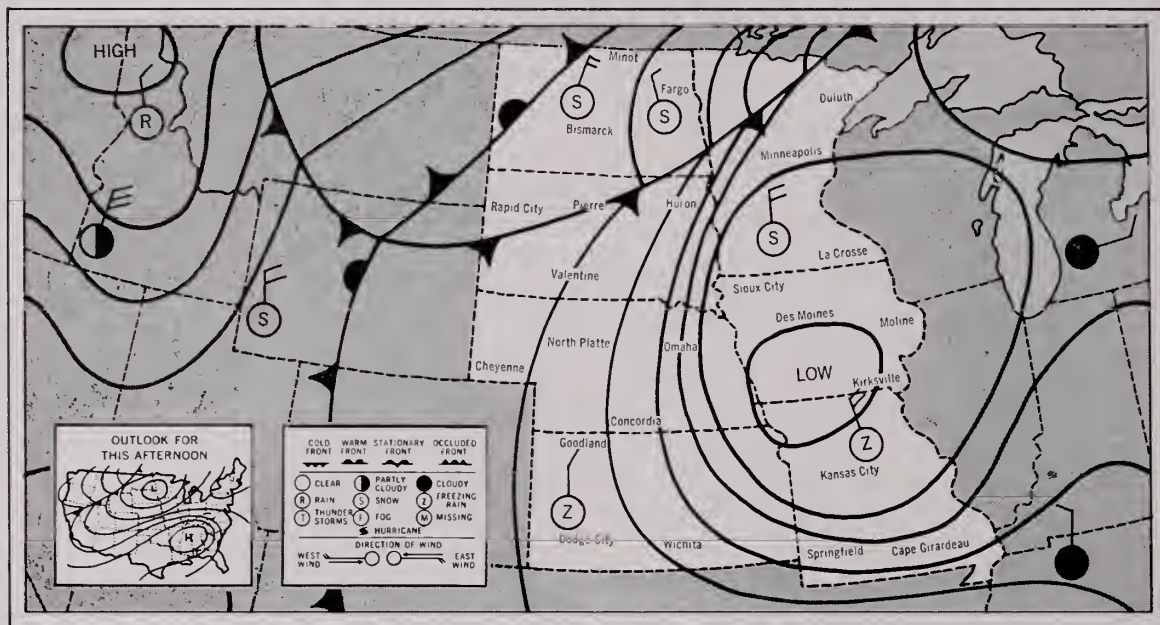
Continued

*Part of the Symposium on Therapeutic Abortion read at the meeting of the Minnesota Obstetrical and Gynecological Society, Rochester, April 23, 1966.

**Liberalized Abortion Laws, Immoral and Dangerous, Medical Opinion and Review.

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does not understand the motivating significance of socioeconomic pressures. He would appear to be responding to a type of moralistic pressure, which in decades gone by led to the legislation of prohibition of intoxicating beverages. I do not consider prohibition a justifiable legislation.

I hear the argument that until the lawmakers change the laws we should not break the existing ones. I would support legal changes, but what changes should be made? If causes for the inevitable abortion are mainly socioeconomic, should the doctors be the only people to make the decisions about individual cases? Should the doctors be involved at all in making decisions, since they would be doing many of the abortions? Should we not legislate a hospital abortion board composed of a doctor, a social worker, and a lawyer knowledgeable in the subject, including specific philosophy pertaining to the indications. This would seem to be far superior to a secretive two-doctor panel. It would have the advantage of consistency, collection of statistics and follow-up studies on a mass scale. After all, does not good legislation mediate liberty, justice, and equality?

Leaving out eugenic reasons for abortions

I believe that the psychiatric indications for abortion are:

1. Severe chronic illness, in any diagnostic category, in which there is usually no reason to expect emotional profit for the mother-child unit.

2. Pregnancy occurring in a never married professional woman above 35 years of age when the woman is clearly unable to deal with this aspect of life, i.e., marriage and child rearing and the shame of being pregnant.

3. Pregnancy occurring as the result of rape or incest, or severe mental illness or mental retardation where the woman cannot be expected to be held responsible for conception, or in the case of incest where the process becomes fixed if not interrupted and the child is stigmatized beyond repair.

4. Recognizing that we cannot separate clearly socioeconomic pressures from psychiatric disturbances, I would include abortion for the woman who has had "too many children," and wishes to do something about it. Here sterilization is also to be considered.

I am not advocating compulsory or forced abortion. It should be an enlightened voluntary matter.

Richard R. Teeter, M.D.
St. Paul, Minnesota

Psychiatric Indications for Therapeutic Abortion*

Con

SINCE WORLD WAR II psychiatrists have oversold themselves. Because of this, many people feel that their skills should be used to solve social, economic, and political problems, and that they should have the right to interpret laws as they see fit. Thus, some psychiatrists have concluded that they can decide who should have a therapeutic abortion, regardless of the law. Bolter¹ abhors this conclusion and states directly and clearly, "Psychiatrists have no more right to break the law than anyone else in our society."

If a decision is made, not on emotions, but

on the basis of medical knowledge only, and within the law, then there are no psychiatric indications for therapeutic abortion.^{2,3} More appropriately, the function of a psychiatrist in this field should be to determine if a patient can tolerate, from the psychiatric point of view, an abortion which is indicated for other than psychiatric reasons, since termination of pregnancy is not without psychiatric risk. Sim³ states, "Abortion, even if therapeutic, may in itself produce a psychosis." Noyes and Kolb⁴ say, "As high as one fifth of the women allowed therapeutic abortions later expressed regret for accepting the procedure."

*Part of the Symposium on Therapeutic Abortion read at the meeting of the Minnesota Obstetrical and Gynecological Society, Rochester, April 23, 1966.

Continued

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In the State of Minnesota the only reason for performing a therapeutic abortion is to preserve the life of the mother or the child. Thus, the principal criteria for psychiatric consideration for termination would be the likelihood of suicide. Interestingly, since the institution of the Maternity Mortality Study in Minnesota there have been only 14 suicides in approximately 1.5 million births.⁵ Statistically this is less than would be expected from any 1.5 million subjects. In a New York City Study⁶ it was observed that proportionally fewer pregnant women commit suicide than those who are not pregnant.

In a British study³ of 1963, which investigated a seven-year period in the City of Birmingham, not one pregnant woman committed suicide. In a California study⁷ of three counties (San Mateo, Santa Clara, and San Francisco) of ten million people in 1961, 1962, and 1963, three instances of suicide by pregnant women were found. This figure was compared with the statistically predicted figure for women of child-bearing age in the three counties. The "actuarial" expectancy of suicide was determined to be 17.6 for the group involved. The explanation of why so few pregnant women commit suicide may be due simply to the fact that pregnant women — including unmarried ones — get considerable more attention from society when pregnant than when not. Studying the case histories of the suicides in the Minnesota study, it is clear in retrospect that the 14 suicides probably could have been prevented if adequate psychiatric care had been obtained and utilized. The most tenable psychiatric diagnoses in these 14 cases are either psychotic depressions or schizo-affective types of schizophrenia, for which there are fairly adequate treatment modalities.

Even though the law in Minnesota now states that the only indication for therapeutic abortion is to preserve the life of the mother or child, consideration should be given to the effect of pregnancy on the future health of the mother, which some authorities wish amended to the law. Noyes and Kolb⁴ state, "Experience does not show that pregnancy and birth of the child in-

fluence adversely the course of schizophrenia, manic-depressive illness, or the majority of the psychoneuroses." Zillboorg⁹ says, "Pregnancies that are marked by psychological tensions, severe moods, and anxieties are not really abnormal pregnancies, and common sense to the contrary, the so-called psychologically uneventful, serene, and sunny pregnancies are apt to be harbingers of severe and even malignant post-partum reactions. This does not mean that all psychologically uneventful pregnancies are forerunners of post-partum psychoses, but they frequently may be — whereas the so-called psychologically stormy pregnancies seldom are such forerunners." He concludes therefore that on purely clinical grounds it is impossible to predict who might and who might not develop a post-partum psychosis. In practice the typical woman who develops such a psychosis is not one who wanted an abortion, but is rather an obsessive, compulsive patient: for example, a married woman with a strong moral code who had a planned pregnancy and who is considered to be a good mother by her peers.

In relation to what occurs post partum, consideration must be given to what happens if a therapeutic abortion is done for psychiatric indications. In a 1965 Swedish study⁹ of 57 cases of abortion (legal, illegal, spontaneous) Jansson reports that psychiatric difficulties were much higher after legal abortions than after illegal and spontaneous abortions. In this study, as in other studies, it appears that those who supposedly need the abortion most for psychiatric reasons develop the most psychiatric complications after the abortion. It could therefore be deduced that those patients who can tolerate a therapeutic abortion do not need it in the first place. In Lindberg's study¹⁰ of 304 patients whose request for therapeutic abortion had been refused, not one committed suicide, although 62 indicated they would if their request was refused. In a series reported by Dr. Hooks¹¹ of Sweden, who investigated 249 cases who were refused legal abortion, there also was not a single suicide, even though seven women

Continued



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in the series had previously made attempts unassociated with pregnancy. He judged that two thirds of the 213 women who bore the children had become well adjusted.

In summary, there are no psychiatric indications for therapeutic abortion because

1. Suicide is less of a risk in pregnancy than in non-pregnant women.

2. It is impossible to predict who will develop a post-partum psychosis.

3. Adequate treatment methods are available to handle psychiatric difficulties occurring during pregnancy.

4. Therapeutic abortion has its own psychiatric morbidity.

Irving C. Bernstein, M.D.
Minneapolis, Minnesota

References

1. Bolter, S.: The Psychiatrist's Role in Therapeutic Abortion: The Unwitting Accomplice. *Amer J Psychiat* 119:312, 1962.
2. As Reported in Medical Tribune, Medical Tribune, Inc. New York, p. 10, Dec. 13, 1965.
3. Sim, Myre: Abortion and the Psychiatrist. *Brit Med J* 145, 1963.
4. Noyes, A. & Kolb, L.: Modern Clinical Psychiatry, 6th Edition, W. B. Saunders Co. Philadelphia & London, p. 99, 1963.
5. Barno, Alex: Criminal Abortion — Deaths and Suicides in Pregnancy in Minnesota 1950-1964. *Minnesota Med* 50:11, 1967.
6. Lane, C. M., as quoted by Rosenberg, A. J. & Silver, E.: Suicide, Psychiatrists, and Therapeutic Abortion. *Calif Med* 102:407, 1965.
7. Rosenberg, A. J. & Silver, E.: Suicide, Psychiatrists, and Therapeutic Abortion. *Calif Med* 102:407, 1965.
8. Zillboorg, G.: The Clinical Issues of Postpartum Psychopathological Reactions. *Amer J Obst Gynec* 73:305, 1957.
9. Jansson, Bergt: Mental Disorders After Abortion. *Acta Psychiat Scand* 4:87, 1965.
10. Lindberg, B.: Svenska Löh-tidn 45:1381, 1948.
11. Höök, K.: Refused Abortion. *Acta Psychiat Scand* 39:168, 1963.

Why Therapeutic Abortion?

DURING THE PAST few decades the medical profession as well as the general public have liberalized their attitudes towards sterilization and the use of contraceptive devices. World-wide attitudes aided by scientific developments have yielded to the pressures of population, economics, and sophistication so that many members of religious groups and sects formerly opposed to these ideas are beginning to accept the new and more reliable forms of contraception. The same pressures are now being brought to bear on our abortion laws. This is not only a medical problem, but a moral issue that eventually will be decided by the populace, led and guided by our religious leaders, doctors, social workers, lawyers and perhaps (overlooked before) mothers.

Since physicians will be the instruments through which the law will act, it is of utmost importance that physicians as a group, obstetricians in particular, play a vital role in determining these inevitable changes. A great deal of credit should be bestowed on the Minnesota Obstetrical and Gynecological Society and particularly essayists in the Minnesota Medicine for their timely and careful study of this problem. They have at-

tempted to rise above the emotional levels involved and to present facts as each individual sees them.

There remain three reasons why a pregnant woman will present herself to a physician for therapeutic abortion: (1) To terminate or avoid harmful effect of gestation and parturition on maternal health, (2) To prevent birth of an unwanted child, (3) To prevent birth of a damaged infant.

Evidence presented in these papers would indicate that widely quoted figures of death due to septic abortion and suicides caused by an unwanted pregnancy have been exaggerated, also that there are few medical conditions that would result in death because of the pregnancy. In spite of this over 60% of the Minnesota Obstetrical-Gynecological Society members and the Minnesota Psychiatric Society members who answered the questionnaire on indications for therapeutic abortion would recommend changes in the Minnesota Statutes as they now read, so that they would include other than maternal life as an indication for therapeutic abortion. Apparently these physicians do not

Continued

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agree with the psychiatrist who believes categorically that there are no psychiatric indications for therapeutic abortion.

Surely the goal of medicine is more than to preserve life. It must be to preserve the life of a person with as little physical and emotional pain as possible. It is no longer possible to separate the psyche from the soma, so one must treat the person as an entity including both of these component factors.

This is a moral, as well as a medical problem. The law, as it now stands, permits an abortion if the life of the mother is in jeopardy. This is perhaps consistent with the quotation from Albert Schweitzer, who states, "Man comes again and again in the position of being able to save or preserve one's own life or life in general at the cost of other life." Everyday instruments of local and federal government make decisions justifying the killing of rioters and other violators of the law to protect the public. It is interesting that in October of this year the Lutheran hierarchy sanctioned the war in Viet Nam where there are as many civilians killed each day as there are military personnel. At the same time the Lutheran hierarchy have sanctioned therapeutic abortion for reasons other than maternal life. In medicine we frequently make decisions involving early termination of pregnancy in various stages of gestation in order to give life to the offspring, sometimes at the cost of maternal life and longevity. Likewise, we make decisions as to whether to enlist palliative measures to make life more tolerable while it lasts. It appears that a consideration of the mother's health, as well as her life as an indication for therapeutic abortion, is an extension of the same philosophy.

The other aspect of this moral problem is that there are many nations in Europe and Asia who do not look at abortion as the taking of a life, for instance, such ethical nations as Japan and Sweden. This history of our own Christian church would indicate that the idea that life begins before fetal activity is relatively a modern one. Saint Thomas Aquinas in the 13th century held that the soul was directly cre-

ated by God and was infused in the embryo, not at the point of conception, but when the embryo was sufficiently formed to receive it. This allowed the medieval church to forbid abortion only after quickening. Pope Gregory V in 1591 designated quickening to occur after 116 days. It is interesting to note that Islam considers life to begin at 180 days of gestation. The exact time life begins, then becomes a matter of definition and not of what is absolutely right or wrong. No one can demand from those who disagree with these indications for therapeutic abortion that they perform an abortion; one could only consent to do an abortion when the criteria to do so would satisfy one's own medical and moral judgment. Conversely, does one have the right to prohibit other ethical people from performing this act, if they consider the act moral and medically indicated and the action is approved legally?

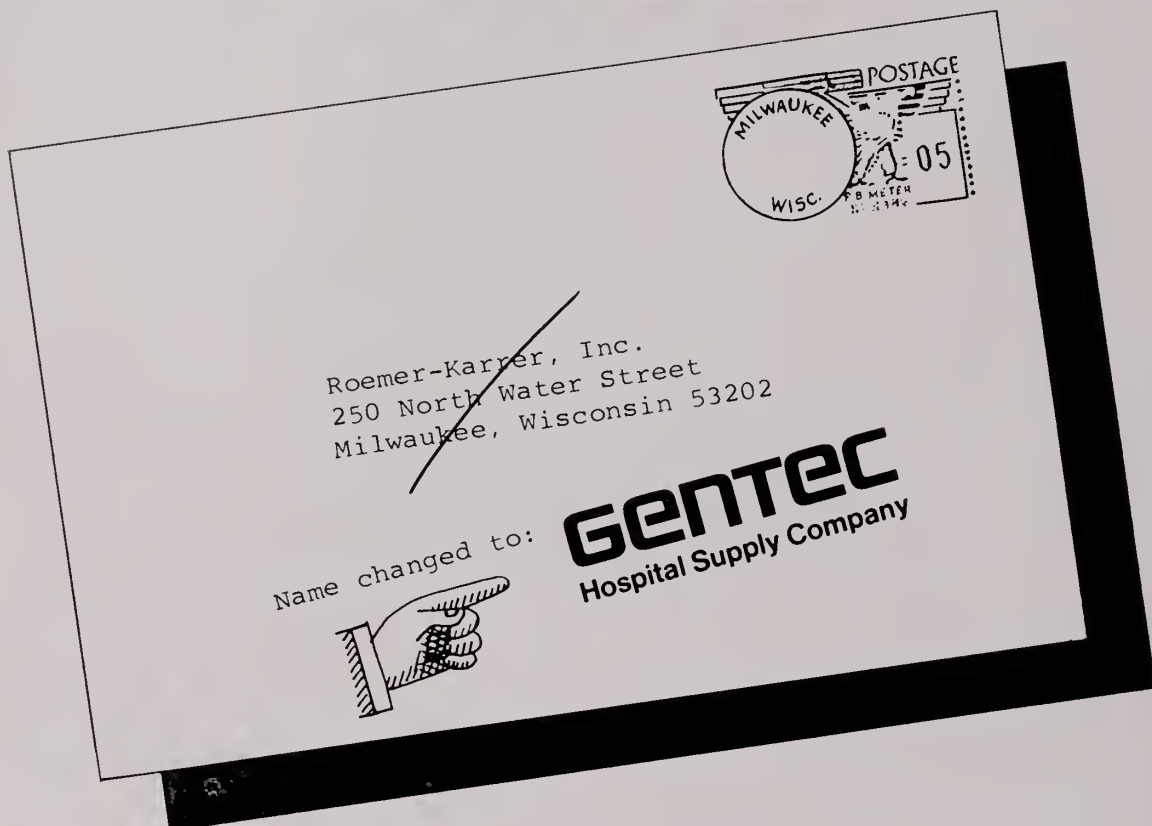
Our present restrictive laws are making hypocrites of physicians who are performing an occasional therapeutic abortion for rape, incest, or pregnancy in children, or for mothers of an unborn child who is likely to be deformed. There are millions of abortions done illegally each year, mostly in married women, that jeopardize the health and life of the mothers. These conditions favor the wealthy who can afford the abortion fees or who can travel to a distant country to have a therapeutic abortion performed in a reputable hospital. It is granted that the law will be difficult to set up in a manner to prevent irresponsibility, but already our sterilization regulations have a pattern similar to that proposed in the penal code of 1954 for abortion.

The need for therapeutic abortions can be greatly reduced by recommending sterilization more frequently when indicated, and by disseminating contraceptive information throughout the world and the United States, making it more available for the needy and indigent people in particular.

Liberalization of our therapeutic abortion laws is inevitable. It is important that physicians have a strong voice in these changes,

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heeding the warnings of the conservatives while recognizing the need for liberalization of therapeutic abortion laws as being realistic for this immediate time and place in our history. I believe this can be accomplished

in a responsible manner without opening the floodgates to indiscriminate therapeutic abortion.

Theodore Watson, M.D.
St. Paul, Minnesota

Thiazide and Aldosteronism

INTERESTING DEVELOPMENTS abound in the field of hypertension. One of the most intriguing is the suggestion by Conn¹ that a sizeable number (1/5th) of patients with unsolved hypertension may have primary aldosteronism (from adrenal cortical tumor). This he deduces from the fact that about 20% of hypertensives have shown a marked reduction of plasma renin,² as in primary aldosteronism.

Hawley and Tobian³ report the interesting observation that administration of thiazide

diuretics to a human with hypertension and an adrenal cortical adenoma precipitated the symptoms of hyperaldosteronism by a severe reduction of plasma potassium, which produced muscular weakness so severe that the patient could not stand up.

All of this suggests that we should not blithely attribute a severe hypokalemia following thiazides solely to the drug, but should alertly look through the pharmacologic veil for an adrenal cortical adenoma.

Rolf Andreassen, M.D.
Minneapolis, Minnesota

References

1. J. W. Conn: Plasma Renin Activity in Primary Aldosteronism. *JAMA* 190:222, 1964.
2. Brown, J. J., et al.: Variations in Plasma Renin Concentration in Several Physiological and Pathological States. *Canad Med Ass J* 90:201, 1964.
3. Hawley and Tobian: *Minnesota Med* 49:889, 1966.

Long-Term Anticoagulant Therapy of Myocardial Infarction

ANTICOAGULATION in acute myocardial infarction has become standard therapy for the hospitalized patient. Only when there exists some contraindication are anticoagulants usually withheld. After leaving the hospital, patients in this area within reach of a medical laboratory are usually continued on long-term oral anticoagulants. However, the value of this long-term therapy is doubtful.

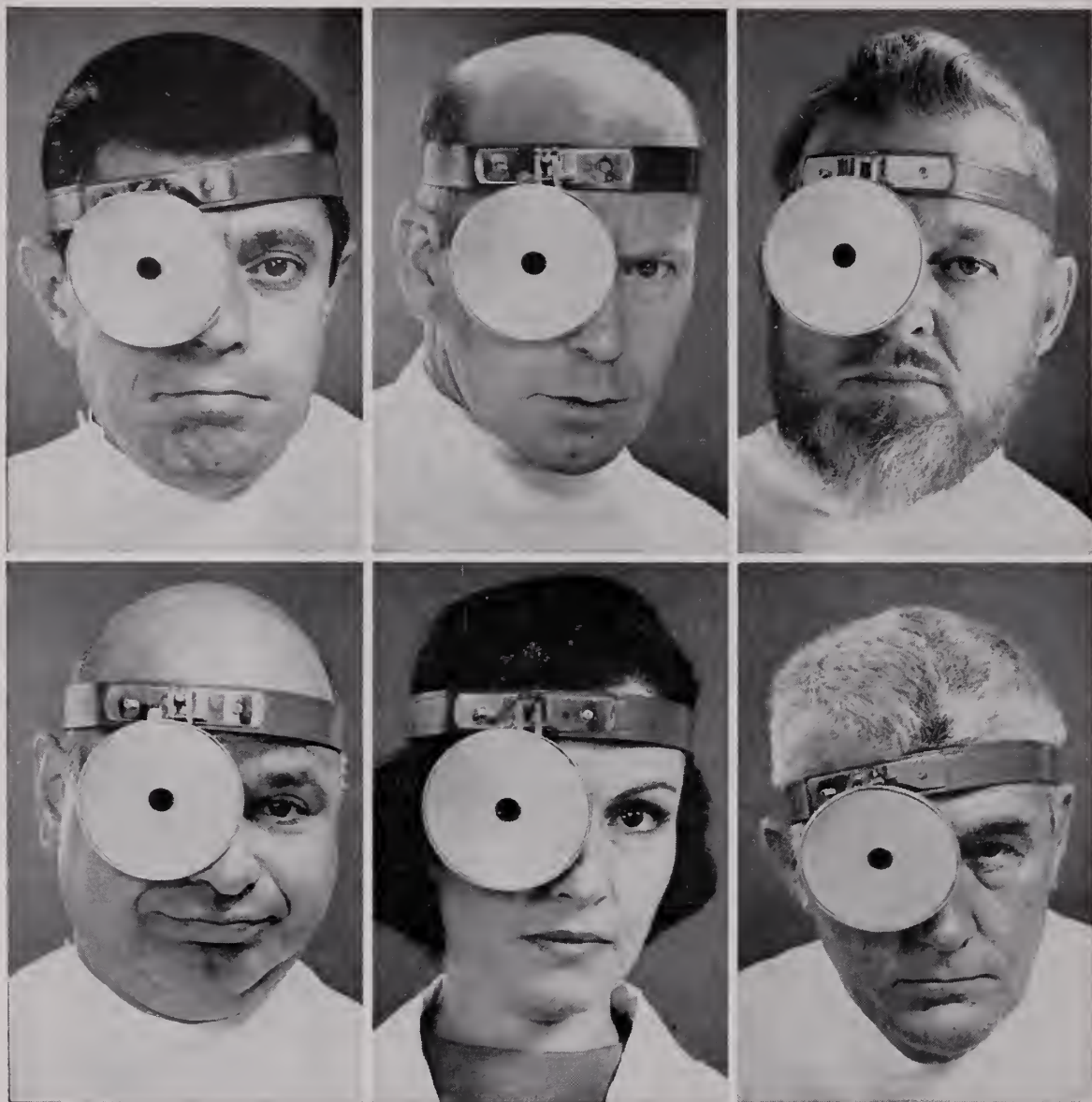
Marple and Wright's study¹ of 800 patients, a controlled series, concerns the first six weeks after myocardial infarction. Their significant findings in favor of anticoagulation cover this early period only and cannot be extrapolated. Bjerkelund's controlled long-term study² shows significant differences in recurrence and in mortality in favor of the dicumarol-treated group only during the first year. Bearman et al.³ show no more favorable mortality in anticoagulated patients after leaving the hospital. The mean death rate after three months for the bal-

ance of a year was 0.03 per cent per day in treated and control groups.

Prolonged anticoagulation bears a load of iatrogenic difficulties. In this journal recently Reece⁴ discussed eight serious bleeding complications of anticoagulant therapy that occurred in one hospital in a period of 18 months.

Askey⁵ mentions cerebral hemorrhage as the most serious of these complications, occurring chiefly in hypertensives; more frequent but less serious were gastrointestinal hemorrhages. Hemorrhagic complications occur within the so-called therapeutic range of increased prothrombin time. There is always a question whether the prolonged prothrombin time is the major factor in a hemorrhagic complication. Often, as in hemorrhages of the gastrointestinal system, an ulcer is demonstrated. The role of the anticoagulant cannot be discounted even though such an

Continued



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Just look at them and you can see how much they have in common. Besides, they all go through pretty much the same training, and pass the same kinds of tests, and measure up to the same sort of standards. Therefore, all otolaryngologists are alike. Right?

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You might also say that all otolaryngologists aren't alike, either.



obvious hemorrhagic source as a peptic ulceration is found. The physician must also accept some responsibility for hemorrhage associated with over-dosage of anticoagulants whether so prescribed or taken in error.

Seaman et al.,⁶ of the University of Oregon, at the American Heart Association meeting October 1966 in New York reported negative results in a ten-year controlled study of the value of oral anticoagulants in long-term post-myocardial infarction therapy. Their study included 255 patients divided into three nearly equal groups: Group A, anticoagulated; Group B, placebo-treated; and Group C, not treated. There was no significant difference in recurrence of infarcts or in death rates among the three groups.

Long-term anticoagulant therapy after myocardial infarction has shown how eagerly these patients accept the regular and frequent visits to their physician. Not the least of the value of such close follow-up is in the field of psychiatry and psychotherapy. The

patient, host to a potentially lethal disease, has overcome it and is doing all he can to prevent its recurrence. It is suggested that physicians consider maintaining the value of the frequent follow-up visits without resorting to the blood-letting ceremony of the prothrombin determination and the exhibition of popular but unproved and possibly dangerous medication.

Currently in many medical centers throughout the United States a large group of post-myocardial infarction cases is being cooperatively studied. In this area this study is under way in Rochester at the Mayo Clinic; at Mount Sinai Hospital, Minneapolis; and at the Marshfield Clinic in Wisconsin. Only patients not currently anticoagulated will be included in this investigation. If long-term anticoagulation therapy is of doubtful value in myocardial infarction, cessation of such therapy within or without such a study is reasonable.

Reuben Berman, M.D.
Minneapolis, Minnesota

References

1. Marple, C. D. and Wright, I. S.: *Thromboembolic Conditions and Their Treatment with Anticoagulants*. C. C. Thomas, Springfield, 1950.
2. Bjerkelund, C. J.: The Effect of Long Term Treatment with Dicumarol in Myocardial Infarction. *Acta Med Scand Supp* 330, 1957.
3. Bearman, J. E. et al.: Myocardial Infarction: Two cooperative clinical studies of therapy. *Med Bull Univ Minn* 37:289, 1966.
4. Reece, Richard L. and Olson, Philip A.: Coumarin Induced Bleeding Complication. *Minnesota Medicine* 49:1677, 1966.
5. Askey, J. M.: Hemorrhage During Long Term Anticoagulant Drug Therapy. *California Med* 104:6, 104:88, 1966.
6. New York Times, p. 68, October 23, 1966.

Unwanted Pregnancies

IN HANDLING unwanted pregnancies, obstacles and complexities soon become apparent which when given contemplative consideration can lead to the conclusion that the problem permits of no single easy solution. The obstetric practitioner discovers early that attitudes toward pregnancy generally may be vagarious and not infrequently in some individuals capricious. An unwanted pregnancy at eight to ten weeks, may at sixteen or twenty weeks become a desirable and an anticipatory one. Variables of this nature are inherent to many normal pregnancies, and would have a greater relevance if, as has been implied, abortion laws should be revised to permit women to be aborted legally at their request.

Dr. Decker* presents a list of the illnesses most commonly complicated by pregnancy and clearly demonstrates that with continuing medical progress the indications for therapeutic abortion will become increasingly narrowed. These and other diseases less commonly complicated by pregnancy involve little if any legal entanglement when the operation is to be performed. Likewise, ethical standards are not violated, and except for certain religious beliefs no moral transgressions are committed.

Therapeutic abortion per se in Minnesota is not hampered by legalities. Within the generality of the law a physician is free to exercise his judgment. Hospitals likewise enjoy this freedom, but for the protection of themselves and their staff members vari-

Continued

*See page 29.



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ous hospitals have established consultative procedures peculiar to therapeutic abortion. Granted that the statute pertaining to abortion could be revised, we doubt that accredited hospitals would change their regulations concerning the procedure. Certain proprietary hospitals might welcome the change, but we are not plagued with such institutions in Minnesota.

When pregnancy is unwanted for social, economic, or whatever reasons other than medical indications, however, the law becomes restrictive. Dr. Lyon* apparently advocates a release from the restrictions and implies that any physician should be free to perform an abortion at any time, for any reason, and designate it therapeutic. He has utilized certain statistics to support his thesis, the accuracy of which we question. For instance the statement "the fact that 20% of all pregnancies are illegally aborted" is in serious error. Although 20% of all pregnancies do terminate in abortion, most of them are spontaneous and may or may not require instrumentation for completion. Also "it is known that between 5,000 and 10,000 women die each year in the United States from—criminal abortions." This statement is without foundation and would be considered ridiculous by statisticians. Dr.

Barno,** working with Minnesota material, fully refutes this. The Minnesota Material Mortality Study is as comprehensive, as complete, and, through its mechanics of gathering and considering statistical material, as authentic as any that can be exhibited by a governmental unit in this country.

Unwanted pregnancy is not a modern problem. It is a predicament as old as recorded history. Nor will the probity of its handling in all cases be forthcoming soon.

English and American jurisprudence has its origin in a consensus of moral precepts which have evolved through Judeo-Christian philosophy. No law will satisfy all nor will the abrogation of a law resolve all problems. Dr. Decker aptly states that "only when we as individuals are sure of real benefit to the pregnant woman can we bring ourselves to interrupt the pregnancy." Our present law—poorly worded as some hold it to be—has served well for the majority of physicians in their obligation to themselves and to their patients. Legalizing criminality in pregnancy would no more solve the problem of unwanted pregnancy than the legalization of trespass and certain misdemeanors would resolve burglary.

Claude J. Ehrenberg, M.D.
Minneapolis, Minnesota

Test Your Word Score

Peccant — *unhealthy, morbidly corrupt* (page 47).

Nakke fornøielse — *Colloquial Norwegian — horses necking for favor* (page 65).

Exophytic — *bush-like; like the head of a cauliflower* (page 70).

Syringomyelia — *a condition marked by abnormal cavities filled with liquid in substance of the spinal cord* (page 74).

Trophoblastic — *pertaining to tissue through which the embryo receives its nourishment* (page 81).

Syncytial — *characterized by a multinucleate mass of protoplasm produced by the merging of cells* (page 84).

Glycogenolysis — *the splitting up of glycogen in the body tissues* (page 90).

Phosphorylation — *the process of introducing the trivalent PO group into an organic molecule* (page 97).

Ethanolism — *addiction to vinyl alcohol* (page 98).

Thioureas — *urea compounds in which sulfur replaces the oxygen* (page 99).

*See page 17.

**See page 11.

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You May Be Right

In the October issue of MINNESOTA MEDICINE appears an editorial by Frederic C. McDuffie, M.D.,* of Rochester, Minnesota, relating to anti-nuclear antibiotic in various diseases. He states that the results of a study by Gokcen, Peterson and Ehrnst are in serious question because they used rheumatic fever patients from several hospitals who were diagnosed by a larger number of physicians. It might be well for Dr. McDuffie to descend from the ivory tower and discover that there are physicians in Minneapolis with no connection with the great fountain heads of learning who are capable of making a diagnosis of rheumatic fever. His arrogant statement is unworthy to appear in your editorial columns.

Geo. R. Martin, M.D.
Minneapolis, Minnesota

*Page 1565 of the October issue.

The Editor's Soliloquy

Name-Dropping in Medical Literature

It may be commendable to cite a long list of authors in medical literature: their works, their specialties, even their biases. It may be still more praiseworthy to be able to say that one has visited their clinics and discussed with them numerous medical and surgical problems.

A short list of references in a scientific manuscript is valuable and lends dignity and authority. It serves as a take-off for an author to slip smoothly into his own monograph. It constitutes the kick-off, as it were, the toss-up, the tee-off, the first serve, the face-off, the "play ball." But when an author copies a list from another author who in turn may have copied from still another author — a progression like the little fleas ad infinitum, then the citation of copious references falls into the category of name-dropping: a common but banal practice running the gamut from the totally naive to the blatantly calculated — the latter reminiscent of the nouveau-riche female whose gown is not just a gown but a Dior and whose hat is not just a hat but a Dache.

Though name-dropping, like its counterparts of table-hopping, back-slapping, apple-polishing, *nakke fornøielse*,* or any of the other methods of currying favor, may appear to be disarming by its casualness, it is nevertheless, a subtle stratagem designed to impress the envious and gullible, to gain vicarious esteem, and to bask in reflected glory. To the discriminating, however, it is all too transparent.

Not that there is anything meretricious about excessive name-dropping, but it patently diminishes rather than enhances prestige and it definitely transgresses the bounds of good taste. Since it is punctiliously avoided by the truly cultured sophisticate, it should be likewise abnegated by the professional man.

Carl O. Rice, M.D.

*See Test Your Word Score, Page 63.

Old Doc Hess says: My man, you're not in hard luck. You can get out and do an honest day's work for an honest day's pay and your hard luck will vanish like magic.

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Curbstone Consultation

Constant Linear Decrease

QUESTION: Between the ages of 20 and 80 you have referred to a constant linear decrease in the systolic wave of the ballistocardiogram, a slower rise of the carotid pulse wave, a linear rise in the time lag between the end of systole and the start of ventricular filling, and the percentage of inert pigment in myocardial fibers: these representing progressive age changes. Is it possible to defer or delay these physiologic changes by maintaining perfect health and condition throughout life?

ANSWER: There is a wide range, at ages 50 to 80, in the individual variation from the median of the age changes in the various items discussed. Some people look 10 to 20 years older at 50; some 20 to 30 years younger at 80 than the average. It is believed most of these are hereditary rather than acquired variations, and only by keeping half of identical twin pairs on differing regimens (minimal exercise, tobacco, optimal vitamin intake for one, the reverse for the other) could one establish any effect of environment on vascular aging. At the moment, the answer to the question would be: cardiac atrophy can be prevented by regular exercise; vascular aging can be hastened by chronic illness.

William Dock, M.D.*
Brooklyn, N. Y.

*Chief, Medical Service Veterans Administrative Hospital.

Benign Stricture of Common Bile Duct

QUESTION: A 50-year-old female has a benign stricture of the common bile duct following a cholecystectomy 3½ years ago. She has now developed esophageal varices. Is there a good medical regimen by which I can manage this patient or should I refer her for corrective biliary tract surgery even in the face of her portal hypertension?

ANSWER: Assuming there are no other factors to contraindicate surgery, such patients should undergo surgery aimed at correcting the stricture. The surgeon will undoubtedly elect to carry out a portacaval shunt at the same time. When corrective surgery is directed at both problems simultaneously one can expect reasonably good chances for success. Since the portal hypertension is the more immediately life-endangering problem, some surgeons would prefer to carry out the shunt procedure prior to the reconstructive biliary tract surgery.

Harold D. Kletschka, M.D.*
Syracuse, New York

*Assistant Professor of Surgery, Chief, Thoracic Surgery (VA) State University of New York.

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1. Schleif, R.H.: J.A.P.H.A., 46:179, 1957 *U.S. Pat. No. 3,062,714

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The Viewing Box

"Bull's Eye Lesion" of the Stomach

A 62-YEAR-OLD white male was hospitalized with the complaints of shortness of breath, easy fatigability, increased weakness, weight loss, anorexia, and tarry stools.

Physical examination revealed a disoriented, emaciated man with axillary and supraclavicular lymphadenopathy, osteoarthropathy, papilledema, and multiple pigmented skin lesions on the back and buttocks. An especially large lesion on the right buttock was biopsied, and diagnosed as superficial melanoma, probably a primary lesion.

On x-ray examination of the stomach, a 5-cm. polypoid, submucosal mass was found (Figure 1 and 2), situated posteriorly, protruding into the gastric lumen, with a 3-cm. ulcer (large arrow Figure 1 and 2) at its apex. Of note was the unusually well demarcated border circumscribing the mass (small arrow Figures 1 and 2). The appearance of the entire lesion was that of a "bull's eye." The small bowel and colon were normal. A chest roentgenogram showed numerous nodules in both lungs (Figure 3).

What is your diagnosis? (See next page.)



Figure 1 (above)



Figure 2 (right top)

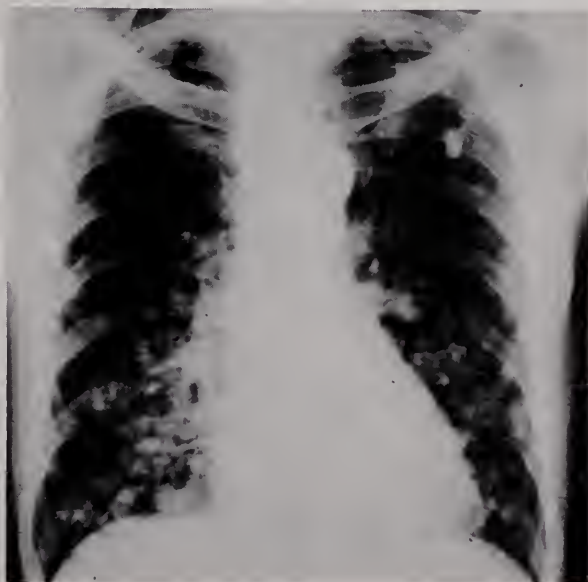


Figure 3 (right bottom)

DIAGNOSIS: Metastatic melanoma of the stomach and the lungs.

From 20-25% of all patients with primary malignant melanoma of the skin, mucous membranes or ocular structures exhibit gastrointestinal metastases either in vivo or at autopsy. In many cases, a gastric metastasis may first draw the clinician's attention to a long forgotten primary. These metastases are equally divided between the stomach and small bowel, the colon being virtually never involved.

Metastatic melanotic deposits to the gastrointestinal tract may present roentgenologically as multiple polypoid lesions occasionally causing intussusception, as submucosal mass lesions associated with partial or even complete bowel obstruction and peritoneal implantation or, thirdly, as gastric ulceration and perforation.

In the stomach, the secondary deposits occur in the body and fundus, the lesser curvature being seldom involved. Willis states that "gastric metastases result from hematogenous dissemination and form localized submucosal masses that grow in an exophytic* fashion to form rigid, saucer-like, polypoid-filling defects. These have a tendency for umbilicated ulceration at their tip, resulting in the central radiopaque area of the target sign when outlined with barium." The central apical ulcerations are almost exclusively seen in the gastric lesions, and seldom in the small bowel lesions, and result from the acidity and the protolytic action of the gastric contents upon the thin layer of mucosa overlying the melanotic deposit. Melanotic deposits to the stomach tend not to infiltrate laterally, accounting for the well demarcated, sharply circumscribed appearance seen on x-ray.

Willis further categorically states that "Unless a meticulous search of every part of the skin, eyes and juxta-cutaneous mucous membrane prove the absence of a possible primary growth, and inquiring elicits positive certainty that the patient has not had any skin lesion which might have been a primary source, the primary visceral origin of a melanoma can not be accepted."

The roentgenological differential diagnosis of a single polypoid gastrointestinal lesion includes spindle cell tumor, lymphoma, Hodgkin's disease, aberrant pancreas, carcinoid, eosinophilic granuloma, carcinoma, and Kaposi's sarcoma. Multiplicity of lesions is rare in any of the above, whereas it is common in melanoma. If target lesions are encountered, say in Kaposi's sarcoma or Hodgkin's disease, they are seldom as large as in melanoma. Further, melanoma is apparently the only lesion characterized by the well demarcated area of radiolucency surrounding the ulcer crater. Finally, the presence of a primary skin or ocular lesion leaves little doubt as to the correct diagnosis.

Eugene F. Binet, M.D.**
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Minneapolis, Minnesota

*See Test Your Word Score Page 63.

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†Department of Medicine, Hennepin County General Hospital.

References

1. Willis, R. A.: *The Spread of Tumours in the Human Body*. 2nd ed. Butterworth. London. 1952.
2. Willis, R. A.: *Pathology of Tumours*. Butterworth. London. 1948.
- 3-7 May be secured from the author.



Neurological Conference

*Carpal Tunnel Syndrome**

Dr. Robert Soll**

This 53-year-old lady was referred to the University Hospitals primarily for a non-neurological problem; however, she also had an interesting neurological complaint which we will discuss today. There is another aspect to this case which we shall consider — that is, the total treatment of the patient. Therapy should not be directed solely at the patient's physical complaints, but rather it must include therapy of the patient's psychological and social needs. In this particular situation the patient finds herself in a hospital far from home. Her relatives are unable to visit her; consequently she has been extremely lonely as well as frightened in these surroundings.

History

Dr. James Zachmant†

The patient is a 53-year-old housewife who was referred to the University Hospitals February 8, 1965, with the complaint of having had several tarry stools early in January, 1965. Prior to this she had been in apparent good health. She had had no abdominal pain associated with this event. The following day her stools were normal, but on the succeeding day her stools again became black and remained so until admission to the hospital. Approximately one week prior to admission she had developed mild epigastric pain which radiated into the chest and upper arms. This pain was worse at night and had no relationship to eating. She did find that drinking milk seemed to relieve the pain; so she placed herself on a milk diet. In spite of this diet, however, her tarry stools persisted. Occasionally she had nausea and vomiting which seemed to be related to the pain. The patient's family physician performed an uppergastrointestinal series but found no evidence of any abnormality in this area. At no time did she vomit blood.

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Held March 4, 1965.

**Department of Neurology, University of Minnesota Hospitals.

†Student Doctor, University of Minnesota Hospitals.

Continued

Another complaint that the patient had when she was seen in New Medicine Clinic was that she had had a decrease in the size of the muscle in her right thumb. She had noticed this only about a week or two prior to coming to the hospital. Recently she also had noted some numbness and tingling in her hands and lower arms on at least two occasions. About two years before this she had noted similar symptoms referable to her hands and arms, but these symptoms cleared spontaneously.

In her past medical history, she had had rather severe infections in her ears as a child. The patient's first husband died at age 50 from a heart attack and she remarried. Her present husband is 56 years old and is farming. He is having some problems with stomach ulcers.

Physical Findings

On physical examination the patient was a frail, middle-aged woman appearing somewhat younger than her stated age. Her blood pressure was 130/85 mm. Hg. and the pulse was 90/minute. She had a slight speech impediment which appeared to be due to rather prominent central incisors. Abdominal examination revealed minimal tenderness in the epigastric area and both subcostal areas. There were no enlarged abdominal masses and the stool examination was negative for occult blood. Examination of her hands revealed a rather marked atrophy of the right thenar eminence. There was a weakness of abduction of the right thumb and of opposition of the right thumb to the little finger. There was no apparent sensory deficit in the hands. The remainder of the neurological examination was normal.

The Systemic Evaluation

Medical Evaluation

Dr. Soll

Has the patient been taking any vitamin-iron preparations that might explain the presence of black stools?

Dr. Zachman: No, she has not.

Dr. Richard Magraw*

Did the abdominal pain occur at night or when she was lying down?

Dr. Zachman

It did occur at night more frequently, but she didn't think it had any relationship to lying down. She described it as a cutting pain rather than a burning pain. Also the pain did not have any relationship to exercise. She had had upper gastrointestinal x-rays and a barium enema which were normal. In addition she has been followed periodically with tests for occult blood which have been trace to 1 plus positive. Since admission she has also had a gastric analysis which was negative for free acid, but histamine provocation did induce free acid. Cholecystography revealed several stones in her gallbladder, and it was felt that this might explain some of her symptomatology.

*Director of Comprehensive Clinic, University of Minnesota Hospitals.

Dr. Soll

The cause of the melena actually has not been found. Certainly the possibility of an ulcer has not been completely eliminated, although I would agree that cholelithiasis may explain some of her symptomatology.

Neurological Evaluation

Dr. Soll

The problem of the atrophy in her right hand was worked up simultaneously along with her gastrointestinal difficulty. When we saw the patient for the first time in Neurology Clinic she had not only atrophy in her right hand but also ankle clonus. This apparent hyperactivity in the lower extremities suggested the possibility of a cervical cord lesion as a possible cause of the atrophy in her hands. In retrospect this ankle clonus may have actually been the result of anxiety and tenseness on the part of the patient. Nevertheless, one of the reasons I had recommended her admission to the hospital was to definitely determine whether a peripheral lesion or a central lesion was the cause of atrophy of the right thenar muscles. I was further faced with the problem of having to explain to her the necessity for her coming into the hospital in order to find out what was causing the trouble in her hands.

Dr. Francisco Baron*

We performed electromyographic studies on this patient and the results were compatible with a diagnosis of carpal tunnel syndrome. There was evidence of abnormalities in both the right and the left hands, but in the right hand, gross atrophy primarily of the abductor pollicis brevis was obvious.

Carpal Tunnel Syndrome

The carpal tunnel is a concavity or canal on the palmar surface of the carpal bones. It is formed by the pisiform bone and the hook of the hamate bone on the medial wall and by the tuberosity of the scaphoid and the crest of the trapezium on the lateral wall. The floor of this canal is formed by the lunate and capitate bones and is converted into a tunnel by a tough, flattened fibrous band, the transverse carpal ligament. Within this tunnel lie the flexor tendons of the fingers and thumb and the median nerve which overlies the tendons. After the median nerve passes through this tunnel, it supplies motor branches to the thenar muscles, the abductor pollicis brevis, the opponens pollicis, and the lateral head of the flexor pollicis brevis. Subsequently the nerve also supplies motor innervation to the first and second lumbricales. Lesions of the median nerve at the wrist, therefore, will affect abduction and flexion of the thumb and opposition of the thumb to the little finger. The median nerve also carries sensation from the volar surface of the thumb and most of the palm of the hand.

Initiating Factors

The carpal tunnel syndrome is not new. The condition was originally described as the "carpal tunnel syndrome" by Marie and Foix¹ in 1913.

*Medical fellow specialist, Neurology, University of Minnesota Hospitals.

Continued

In 1933 Abbott and Saunders² noted that aching and trophic changes preceded the sensory deficit. In 1947 Brain³ proposed that extension of the wrist compressed the nerve. Since many of the household tasks required extension of the wrist, he felt that this position was the likely cause of this syndrome. Many other authors have studied this problem, and the current concept is that flexion of the wrist is the principal cause of damage to the nerve. It is felt that the median nerve is subjected to compression between the flexor tendons and the transverse carpal ligament by flexing the wrist. This theory is still subject to some speculation, however, and some authors have claimed that there is a non-specific synovitis involving the synovial membrane in the carpal tunnel.

Many conditions have been related directly or indirectly to the carpal tunnel syndrome. This syndrome has been encountered most frequently in post-menopausal women; also it has been seen in myxedema, pregnancy, endocrine disturbances such as acromegaly, and amyloidosis. There is a low incidence among male manual laborers.

Clinical Observations

As far as the clinical diagnosis of this syndrome is concerned, the history will often reveal symptoms of pain, burning and tingling in the hands as some of the initial complaints. This pain will be limited to the two lateral fingers and thumb as a rule; occasionally, however, there may be radiation of pain into the upper arm and at times into the shoulder. The pain usually increases during the night and may wake the patient. Swelling and numbness of the fingers may occur and some patients note an inability to use the thumb due to weakness of the thenar muscles. They do complain of dropping articles which they are holding or of an inability to make full use of their hand. The typical patient with this syndrome is a middle-aged housewife whose dominant hand has been affected for about a year or longer. Interestingly, the carpal tunnel syndrome was initially studied as a disease confined to females. Many studies have found both sexes affected; for example, one reported by Phalen and Kendrich,⁴ 1957, cited 71 cases in which 54 cases or 76% were female and 17 or 24% were male. The age of occurrence of this syndrome is usually between 30 and 60 years. Most frequently the disease is bilateral; of the 71 cases cited above, 39 were bilateral and 32, unilateral. Of the latter 32, 23 involved the dominant hand. The differential diagnosis includes cervical osteoarthritis and herniated cervical disc, syringomyelia,* progressive muscular atrophy, trauma of the spinal cord or nerve roots, tumor or aneurysm of the cervical cord and the cervical rib syndrome.

Physical Findings

Physical findings in this condition will usually reveal atrophy in the abductor pollicis brevis; subsequently, the opponens pollicis and the flexor pollicis brevis may become involved. Sensation may be diminished over the distribution of the median nerve in the hand and fingers. In 85% of these patients percussion of the median nerve at the wrist will often elicit a sensation of tingling in the hand. This is Tinel's sign which indicates a partial lesion or early regeneration in a peripheral nerve. Experience in the interpretation of this sign is necessary because percussion of the median nerve at the wrist in a normal individual may also produce tingling

*See Test Your Word Score Page 63.

in the hand. Another special test which may be performed is the so-called "wrist flexion test." Hyperflexion of the wrist for approximately one minute will induce or accentuate numbness or paresthesias in the hand. This test may be positive in approximately 75 to 90% of the cases. X-ray examination of the wrist has been negative in approximately 95% of the cases but may be positive in those instances in which a skeletal abnormality exists as a result of a fracture of the wrist or arthritic process. Another special diagnostic procedure is the aggravation of the paresthesias in the hand by means of a blood pressure cuff applied above the level of the elbow with the pressure exceeding the systolic blood pressure. Weakness of the thumb may also be increased by this maneuver. Finally the electrodiagnosis of this condition is also being used since it has been positive in approximately 95% of cases. This is a particularly valuable procedure in the early stages of this condition at a time when surgical therapy will have the best chance of success. In mild cases numbness and atrophy are not always found; the patient may be complaining only of paresthesias. In this event a diagnosis of neuritis is often made empirically without discovering a definite cause. The conduction latency of the median nerve across the wrist may be the only objective finding.

Electromyogram Findings

The electromyogram has been employed for the past 20 to 25 years for the diagnosis of this condition, although it has been in wide use for only the last few years. We perform three tests: the conduction velocity of the median nerve across the wrist; the recording of the denervation potentials in the muscles of the thenar eminence; and finally, the conduction of sensory stimulation from the first finger to the median nerve at the wrist. Related to the motor conduction velocity, the median nerve is stimulated above the wrist and the conduction latency is recorded from two electrodes in the muscles of the thenar eminence, one in the abductor pollicis brevis and the other in the proximal phalanx of the thumb. A normal conduction delay is between 3 and 5 milliseconds. *In the presence of carpal tunnel syndrome the conduction latency exceeds 5 milliseconds.* In patients with severe atrophy of the thenar muscles, it is necessary to insert a coaxial needle electrode to record the conduction velocity; however, sometimes it is impossible to obtain a muscular response. In these patients the physical signs are far advanced and the diagnosis is not a problem; or, in unilateral cases there is often a prolonged conduction delay in the contralateral median nerve.

In the second part of the test, the electromyographic examination of the thenar muscles may be helpful in verifying denervation potentials and *reduction in number of the motor units which can be activated voluntarily.* Fibrillation potentials are not commonly seen in the carpal tunnel syndrome.

The third test that is performed in the electromyographic examination is sensory conduction. Ring-stimulating electrodes are placed around the index finger and two surface-recording electrodes are placed about the wrist. Subsequently this process is reversed and stimulation is applied above the wrist and the signal recorded from the index finger. *Patients with carpal tunnel syndrome tolerate a higher degree of stimulation than*

Continued

do normal patients. The action potential is reduced in size, and the latency which is normally between 1.5 and 3.0 milliseconds is delayed 4.0 to 5.5 milliseconds in patients with carpal tunnel syndrome.

Dr. Soll

The surgical carpal tunnel release was performed bilaterally in this patient by the orthopedic surgeons. This is usually accomplished by sectioning the transverse carpal ligament which decompresses the median nerve in the carpal tunnel. I have had made 35 mm. slides of this patient's hands which demonstrate the atrophy of the right thenar eminence as well as the site of the surgical procedure. I would like to emphasize that this particular neurological condition is one in which considerable improvement can be obtained if the diagnosis is made relatively early. On the other hand, considerable incapacitation can result, especially in those persons who depend on the use of their hands, if treatment is delayed.

Psychological Evaluation

In this patient we do have another problem aside from her physical complaints. She finds herself in a large hospital full of strange faces and quite far from home. In addition to this she may have significant problems at home which cause worry and anxiety. Her recovery may be delayed by these factors and thus prolong her total length of hospitalization. Therefore, it is the responsibility of the hospital staff to understand their patients thoroughly, so that the patients' morale as well as their physical disabilities can be improved. In this way their period of confinement may be shortened. Dr. Brantner will discuss this particular patient's psychological evaluation and tell us what significance it has in our total treatment of this patient.

Dr. John Brantner*

The patient is a very interesting person psychologically. On the Minnesota Multiphasic given by the psychometrist she appears to have a relatively mild neurotic adjustment with numerous physical complaints. She is moderately depressed, withdrawn, and introverted at the present time. I visited her myself and found her to be extremely diffident. She didn't actually refuse, but she clearly did not wish to take any of the tests; so I set them aside and started chatting with her. At the beginning I gave her one very quick intelligence test and found a mental age of 11 years. This was considerably lower than expected but there was one interesting aspect: the test consisted of 10 questions such as "give me the names of some fishes; tell me what houses are made of; give me the names of some big cities." She asked, "Do you mean any cities?" She then proceeded to answer, "New York, London, Toyko, Chicago, San Francisco and Los Angles." To name cities outside of the United States is extremely rare in mentally deficient or dull people, and this did not coincide with the other results of the tests. She is a very shy woman and expresses a great deal of self depreciation. I hope Miss Baker will give us some idea as to where this might have originated. This is the patient's first hospital experience in her 53 years. She is very frightened. After conversing with her for almost an hour I talked her into taking another fairly good quick test:

*Associate professor, Clinical Psychology, University of Minnesota Hospitals.

the Binet Vocabulary, which revealed an IQ of approximately 122. So she is an intelligent woman but one whose expression of this intelligence is marred by extreme diffidence. I went to see her again after she had had surgery. Today and yesterday she has been in considerable discomfort physically. I will continue to see her daily, at least until her family is able to be here.

Dr. Soll

There is often a great tendency for us to hasten through our examinations and treatment of patients without devoting time to their emotional needs. What you have said of this patient so far indicates that she is very much in need of reassurance and encouragement.

Social Service Evaluation

Miss Annie Laurie Baker*

This woman lives about 25 miles from where she was born in a rich farming community. In the State of Minnesota there are little pockets of foreign groups and she belongs to one of them. Her father came from the German border very near Switzerland and her mother lived in a little village near Zurich. They were married rather young and then moved to an area in Minnesota where there were a great many Swiss people. When she was a little girl she spent most of her time working outside with animals. Now she raises chickens. She noticed that she was beginning to have trouble with her hands when she was picking off the feathers. It is very important to her that she retain the use of her hands. She spent most of her young life by herself because she was the only girl with three brothers. She said that until she came to this hospital there probably had never been a day in her life that she had not been outdoors. When asked about school she stated that she was "real dumb," but she went through high school. She has been married twice but has never had any children.

She has been very worried here in the hospital. One concern is her 86-year-old mother who does all her own cooking and housework. Prior to her illness the patient visited her mother about twice a week to assist her with the housework and baking. She had asked several of her friends to look in on her mother while she was away. Also she is very concerned about having cancer. Her first husband had cancer and was treated at the Mayo Clinic. The pains in her chest and abdomen she thought were similar to his. Following his death, the patient married again. She owns the farm they live on which consists of 180 acres. They have done very well and have no big bills. During the last few years her present husband has had a nervous breakdown, which has concerned the patient as well as his family. I gathered from her remarks that they think he may be suicidal. It was difficult to learn anything more definite about his illness because the patient did not want to talk about it. Her husband also has an ulcer condition for which he is being treated. In summary, I thought she was a well integrated person although she is very depressed and has three very serious worries: she is worried about having cancer; she is worried

*Director, Social Service, University of Minnesota Hospitals.

about her husband; she is worried about her mother. For these reasons, she is very anxious to go home.

Discussion

Dr. Richard Magraw

We do a good deal of talking with students about paying attention to the whole person. Here is a good example of how easy it is for us to focus on the immediate problem that we are concerned about, thus losing sight of the fact that this "problem" is a minor incident in the patient's total life experience. For example, she has a husband at home who is suicidal. I think doctors are asking for a rather inconsequential role, if they fail to take into account the actual picture. One question I would like to ask about the neurological problem: how urgent was it to have this carpal tunnel release done? Which of the two medical problems is really of more concern, the melena or the atrophy of her hands? I would guess that probably the atrophy would not have been as pressing as the melena, but maybe I am wrong.

Dr. Soll

As things turned out, certainly the melena was the more immediate problem; however, had the patient been found to have a cervical cord lesion, very likely the neurological problem would have been the more important of the two. Nevertheless, both problems needed to be taken care of while she was here. As far as the urgency of performing a carpal tunnel release is concerned, the sooner it is done, the better.

Dr. Magraw

I would like to ask Dr. Zachman if he feels that the cause of the melena has been found or whether further diagnostic studies should be done?

Dr. Zachman

I don't see how the question of melena has been fully answered. She has had continued trace of 1+ guaiac tests throughout her hospital stay — in spite of the fact that all studies to date have been negative.

Student Doctor

A guaiac test showing a trace to 1+ is within normal limits, particularly if a patient is eating meat.

Dr. Soll

There may be many obscure causes of bleeding and resultant melena. In spite of the fact that our tests thus far have been negative I think it would be well to continue to watch for further evidence of melena; then further investigations will have to be made.

Summary

We have discussed a 53-year-old housewife who has presented an interesting complex of problems, both organic physical complaints and problems which developed due to her emotions and personality while she was in the hospital. On the one hand, she presented both a neurological problem which proved to be readily diagnosed and treated and a gastrointestinal problem which has not been as easily resolved. Although

cholelithiasis was found and could partly explain her epigastric symptomatology, it does not readily explain the presence of melena which the patient had significantly prior to her admission to the hospital. She was placed on a ulcer diet which did partially relieve her symptoms. It will be important in the future to continue to follow the patient in order to determine whether further symptomatology does occur which would require renewed testing. On the other hand, this patient also has impressed upon us the necessity for our being aware of all of her problems, both her immediate medical problems as well as her problems at home. Resolution of the latter certainly may play a significant role in the satisfactory recovery of the physical problem for which she is being treated in the hospital.

Robert W. Soll, M.D.
University of Minnesota Hospitals

References

1. Marie, P., and Foix, C.: *Rev Neurol* 26:647, 1913.
2. Abbot, L. C., and Saunders, J. B.: *Surg Gynec Obstet* 57:507, 1933.
3. Brain, W. R., Wright, A. D., and Wilkinson, M.: *Lancet* 252:277, 1947.
4. Phalen, G. S., and Kendrick, J. I.: *JAMA* 164:524, 1957.

Participating in the conference were: Student Doctor James Zachman; Dr. John Brantner, Associate Professor, Clinical Psychology; Miss Annie Laurie Baker, Director, Social Service; Dr. Francisco Baron, Medical Fellow Specialist, Neurology; Dr. Richard Magraw, Director, Comprehensive Clinic and Dr. Robert W. Soll, Department of Neurology. (All from the University of Minnesota Medical Center)

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Keep pace with the traffic. Slow driving on high-speed roads is dangerous.

Drive defensively. Watch for drivers signalling, and watch for those who don't signal.

Watch traffic around you. Be on guard for changing conditions.

Watch for traffic hazards, obstructions, breakdowns, merging traffic.

Check your speed often. You may be going faster than you think.

Reduce speed if driving conditions drop below standard.

Stay in the proper lane. Don't straddle the dividing line.

Obey posted rules and watch for route signs along the way so you will be in the proper lane to make changes without endangering traffic behind you.

At NIGHT drive at speeds that give you stopping distance within the range of your headlights.

Dim your lights when approaching cars going in either direction; this rule applies even if the highway is divided by a median strip.

*See *Minnesota Med* 49: 1761, 1966.

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Medical Seminar

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THE TERM trophoblastic* disease is elusive, for its limits are poorly defined, to say nothing of its included entities. The true trophoblastic tumors — hydatidiform mole (benign mole), chorioadenoma destruens (invasive or destructive mole), and choriocarcinoma or chorioepithelioma — are described in current textbooks.

Hydatidiform Mole

The hydatidiform mole is a bizarre complication of about one of 2,000 pregnancies in the Western World and of more frequent occurrence in underdeveloped areas, specifically Formosa,^{1,2} the Philippines,^{3,4} and Mexico.⁵ In two series^{2,3} the incidence was reported to be as high as one in 82 pregnancies and one in 131 female autopsies. Although this high incidence could possibly be related to poverty and poor diet, Douglas⁶ has reported no increased incidence among the indigent population treated at Bellevue Hospital. A consistent finding has been that the mothers in the Asiatic studies are older and have more children.

Etiology

The cause of the hydatidiform mole is undetermined; the possibility of a filterable virus has been virtually eliminated.⁷ Repeated molar pregnancies occur, and Husel⁸ recently described a woman who had six consecutive molar pregnancies; he also cited another who had 18. It has been suggested that molar pregnancy is the result of re-

tention of an early abortion; however, this may be the effect rather than the cause.

Clinical Manifestations

Clinically, a molar pregnancy becomes manifest in the second trimester, most often around the eighteenth week.⁹ The patient may pass tissue, or she may present with excessive vomiting, bleeding, or toxemia, or any combination of the three. As many as 35% of patients with hydatid mole have toxemia.⁵ On examination, the uterus is usually larger than it should be considering the period of gestation and feels "tensely elastic" rather than soft.²

Diagnostic Tests

Naturally, no fetus will be detected by clinical or laboratory means, unless a twin pregnancy exists. Our British colleagues have become so astute at diagnosing the hydatidiform mole with sonar that Harper and MacVicar¹⁰ diagnosed such a twin pregnancy before the induction of labor. One or both ovaries may be enlarged, representing theca lutein or compound lutein cysts. The latter term is preferable since luteinizing granulosa cells may be part of the cyst wall.¹¹ There is some evidence that if compound lutein cysts occur after a mole is formed, there may be less of a tendency for malignant change.⁹ If a quantitative pregnancy test is done, the results will be greatly elevated. The normal limits of the test as described by Delfs¹² show that the value, which peaks at about the seventieth day, should be less than 700,000 international

*See Test Your Word Score Page 63.

Continued

units and, after the one-hundredth day, it should be within 3,000 to 30,000. In multiple gestations, the downswing will be delayed about a month. The diagnosis may be confirmed only when grape-like tissue is passed. Microscopically, there are villi with edematous and degenerated stroma but without blood vessels; the trophoblast shows varied degrees of proliferation. The microscopic picture probably is of little help in determining prognosis. Since the hydatidiform mole is avascular, only the villi adjacent to maternal circulation show cellular activity; yet these villi are the ones frequently missed on curettage.

Treatment

About 80% of molar pregnancies are uncomplicated after delivery. Usually delivery is accomplished with oxytocin stimulation, but uterine rupture has been reported.¹³ Hysterotomy is commonly used if the fundus is above the umbilicus. The use of hypertonic glucose has been reported.¹⁴ After delivery curettage should be performed; the physician must be cautious not to perforate the softened uterine wall. Perforation at such a time has been suggested as a cause of chorioadenoma destruens.^{15,16} Hysterectomy is recommended as the treatment if the patient has completed her family or is more than 40 years old; the Asiatic studies indicate that mothers who are more than 40 years old have a higher risk of developing malignancy.

Follow-up Studies

Quantitative pregnancy testing is the best method of follow-up to determine the trend of the titer of human chorionic gonadotropin. According to the observations of Brewer and associates,¹⁷ a decision probably should be made at 60 days after the mole has been evacuated, if the titer is rising or has remained constant. Naturally, dilatation and curettage should be done before this time if the patient has persistent vaginal bleeding. Uterine scrapings are often of no help; thus laparotomy or biopsy of metastatic lesions, if present, is necessary to establish a tissue diagnosis. Unfortunately in an effort to make this diagnosis, the phy-

sician may deprive the patient of future childbearing or may spread tumor cells and expose the patient to operative morbidity and possibly mortality. That sterility is not a necessary result has been shown by Wilson and associates,¹⁸ who removed isolated nodules from the uterus in selected cases. Hertz and co-workers¹⁹ and Brewer and associates,¹⁷ however, divided trophoblastic disease into nonmetastatic and metastatic and treated patients who had metastasis according to the value of the human chorionic gonadotropin titer alone. In doing so, they obviously are treating chorioadenoma destruens as though it was truly malignant.

Chorioadenoma Destruens

Perhaps a better term for this intermediate type of trophoblastic tumor would be destructive or invasive hydatidiform mole, for that is exactly what it is. When it occurs, chorioadenoma destruens always forms from a benign mole; contrariwise, about one of six benign moles becomes invasive. Microscopically, the villous architecture is retained, even in metastasis, although it may be hard to find. This is the only feature that differentiates invasive mole from choriocarcinoma, as both may cause persistent vaginal bleeding, compound lutein cysts, increased human chorionic gonadotropin titer, and metastasis. In cases of invasive mole, metastasis occurs most commonly to the uterine wall by direct extension and to the lung or vagina via the bloodstream. The prognosis is excellent, however, even in metastatic invasive mole because removal of the primary tumor cures virtually all of these patients. However, this benign metastasizing tumor may indirectly kill by hemorrhage or sepsis. One such death has been reported.²⁰ Chemotherapy will effect a cure in cases of this tumor.

Choriocarcinoma

In a discussion of choriocarcinoma, Hertz' analogy of trophoblastic disease lying on a spectrum can be considered.²¹ However, if this analogy were entirely true, invasive moles could be expected to progress to choriocarcinoma. In fact, it is the end result

of only about 3% of benign moles. About one half of the cases of choriocarcinoma result from moles, one fourth from abortions, and one fourth from normal pregnancy. Ectopic pregnancy accounts for about 2%.⁹

In undergoing this malignant change, the trophoblast loses its villi, and there is anaplastic overgrowth in varied proportions of both layers of trophoblast. There is invasion of maternal tissue, with coagulation necrosis and hemorrhage. Since this cancer is entirely dependent on free maternal blood for sustenance, the tumor nodules frequently are hemorrhagic and have necrotic centers.¹¹

Treatment

The method of treatment varies with the philosophy of diagnosis. Some physicians institute chemotherapy after histologic diagnosis, usually after hysterectomy. Others will institute treatment in cases of a persistent titer, considering the condition to be one of metastatic trophoblastic disease; they reserve surgery for unresponsive cases.

The customary chemotherapy initially includes the use of methotrexate, a "course" consisting of 25 mg. per day for five days, either orally or intramuscularly administered. Morbidity from the drug is frequent and can be monitored by means of clinical examination and the usual laboratory tests, especially leukocyte and platelet counts. The patients under treatment should be examined at least once daily for oral lesions, alopecia, reddening of old scars, or neuropathy. Death occurs infrequently and then usually only after repeated courses. That normal pregnancy is possible during the period of remission has been cited by Brewer and associates,¹⁷ McKelvey,²² and Freedman and co-workers.²³ Tumor response may be monitored each week by means of a sensitive, quantitative pregnancy test. The courses of methotrexate are repeated until toxicity is prohibitive or until the human chorionic gonadotropin titer falls to zero. When the human chorionic gonadotropin titer reaches zero, Brewer and his associates¹⁷ give two more courses to ensure remission. A promising adjuvant to metho-

trexate is actinomycin D; this drug is given intravenously at the first sign of resistance to methotrexate in a dose of 10 μ g per kg. per day for five days. Hertz and associates²⁴ reported 17 cases of methotrexate failure in which treatment with actinomycin D was used; in the 17 cases, 10 remissions were noted. Ross and colleagues²⁵ recently cited 19 patients who were resistant to methotrexate; nine of these experienced remission after use of actinomycin D. Using the drug as a primary treatment, mainly because hepatic dysfunction obviated methotrexate therapy, these authors noted remissions in three of seven patients and in eight of 14 patients in two series. Triple therapy (5 mg. of methotrexate plus 10 mg. of chlorambucil orally and 0.5 mg. of actinomycin D intravenously daily for five days) has been used in patients unresponsive to either methotrexate or actinomycin D alone.

Prognosis

Ross and associates²⁵ believe that the patient's prognosis is vastly improved if the duration of disease is less than four months and if the human chorionic gonadotropin titer is less than one million when treatment was begun.

Survival statistics are difficult to evaluate because methotrexate has been in use for only about 10 years and because investigators do not share common diagnostic criteria. For example, Ross and associates²⁵ stated that they observed remission in 76% of their cases of choriocarcinomas and in 73% of their patients with "chorioadenoma destruens and mole." Cure in the latter group is theoretically 100%. The former group probably includes cases of invasive mole. Since invasive mole occurs five times more frequently than does choriocarcinoma, the question arises concerning how many patients with truly malignant tumors are being cured. In general, about two thirds of patients with choriocarcinoma experience remission after methotrexate therapy.^{4,21,26} About 10 to 20% more respond to actinomycin D, although experience with this drug is limited.

Continued

Metastases

Pulmonary metastases in choriocarcinoma generally assume three forms.²⁷ Most frequently, discrete asymptomatic lesions are found on roentgenograms of the chest; some of these patients have painless hemoptysis. However, the roentgenogram may have a "snowstorm" appearance, which is often associated with an asymptomatic condition but an ominous prognosis. Finally, a tumor mass may embolize, with symptoms and signs typical of pulmonary embolism. The embolism may be the presenting picture, after which the malignant embolus invades. Cerebral metastasis is frequently fatal and also indicates probable resistance to chemotherapy, although there is evidence that radiation may be of benefit.²⁴

Other Trophoblastic Disease

The gestational trophoblastic tumors are only a part of the group of trophoblastic diseases and form a spectrum of disease entities. Toward the benign end is syncytial* endometritis. Although this condition probably is benign, its name indicates that it is a trophoblastic disease. Novak and Woodruff¹¹ described histologic persistence of syntrophoblast and inflammatory cells at the placental site after abortion or normal delivery. Indeed these cells may even be seen in single file between myometrial fibers, but there is no hemorrhage or necrosis. Apparently this condition must regress, for no one has described the fate of these cells.

Along the trophoblastic continuum is embolization of trophoblastic cells during a normal pregnancy. This paradox of nature was described almost 80 years ago, and the problem is yet to be solved. This potentially malignant tissue embolizes in about one half of normal pregnancies²⁸ (and probably also in aborted and molar gestations) and regresses spontaneously. If the cells retain viability and invade, they appear the same microscopically and ultrastructurally; yet the tumor is a choriocarcinoma. In any event, this process is included in trophoblastic disease because it has not been reported in 100% of maternal autopsies and

because the normal place for trophoblast is within the uterus.

In a sense, gestational choriocarcinoma does not represent the most malignant form of trophoblastic disease, since it is at least responsive to medical therapy. At the malignant end of the spectrum are testicular choriocarcinoma and teratomatous choriocarcinoma. These lesions are as aggressive as the gestational form but are refractory to any chemotherapy²⁹ and cause death virtually 100% of the time.

Current Research

There are many areas of research into the trophoblastopathies. In the field of immunology, Breyere³⁰ has devised a most provocative experiment. Groups of female mice from one inbred strain were mated with each of three different inbred male strains. Then tumor tissue from two of the male strains was transplanted into each postpartum female and into virgin females (as controls). The tumor was completely accepted (even as late as 200 days after delivery) only in those females whose mates and tumor transplant came from the same strain (Table).

TABLE
Rejection Patterns of Tumor Tissue Transplant in
Female Mice of Same Inbred Strain

Tumor Tissue From	Postpartum				Control No Mating
	Male Strain	Mated With A Strain	Mated With B Strain	Mated With C Strain	
A		Accepted	Rejected	Rejected	Rejected
B		Rejected	Accepted	Rejected	Rejected

Immunologic Tolerance

Since neoplasms can overcome small barriers to immunity, the experiment was repeated with the use of skin grafts. The results were the same, except that the skin grafts were rejected after prolonged periods of time. Three or more pregnancies provided these females with maximal immunologic tolerance; fewer pregnancies resulted in earlier rejection of the grafts. This increased tolerance may be the reason why multiparity predisposes to choriocarcinoma.

Choriocarcinoma is well known for its

*See Test Your Word Score Page 63.

occasional spontaneous regression. Also, women have been known to die from choriocarcinoma and yet have no primary tumor remaining in the uterus.¹¹ Perhaps some form of total or partial body immunity is acquired in these cases. Pierce and co-workers³¹ have shown that human choriocarcinoma from both males and females transplanted to hamsters behaves identically in growth and response to drugs. Therefore, the clinical response to methotrexate may represent the summation of the female's partial immunity to the trophoblast and the drug effects. However, trying to heighten the mother's immune response, with or without chemotherapy, has been unrewarding.^{32,33}

Patients with choriocarcinoma have increased tolerance to repeated skin grafts from their husbands. Ben-Hur and associates³⁴ have, therefore, recently suggested that, for a screening test, a woman with hydatidiform mole be given a small graft from her husband; if the graft is rejected, supposedly malignancy will not develop. Paradoxically, Mathé and co-workers³⁵ have found that patients with this increased tolerance frequently have increased antibodies against the leukocytes and platelets of their spouses. This immunologic disparity between tissue and serum is unexplained.

Consanguinity

Consanguinity has been discovered in three cases of choriocarcinoma in Beirut.³⁶ The author suggested that intermarriage is relatively common in Eastern Asia and may account for the high incidence of the malignancy.

Pathologic Findings

Interesting pathologic findings have emerged recently. Electron microscopic studies of gestational and nongestational choriocarcinoma have found them virtually identical in every respect.³⁷ Also normal pregnancy, mole, and choriocarcinoma all have identical trophoblastic patterns as seen under the electron microscope. During these studies it was found that human chorionic gonadotropin was produced by the syntro-

phoblast, not by the cytotrophoblast,³⁸ and that the syncytium is derived from cytotrophoblast.³⁹ Sex chromatin of choriocarcinoma may be either male or female, regardless of which sex harbors the tumor.²⁸

Chorionic Gonadotropin or Pituitary Gonadotropin

The possibility exists that human chorionic gonadotropin may differ from pituitary gonadotropin. Schwartz and Mantel⁴⁰ in experiments with rabbit antisera could not account for 20% of the human chorionic gonadotropin. They postulated that it was an immunologic variant not present in pituitary gonadotropin, but they could not identify it. However, the bulk of evidence⁴¹ seems to indicate that the gonadotropins from the two sources are identical, both immunologically and biologically.⁴² Human chorionic gonadotropin from normal and molar pregnancies may be identical except for minor antigenic differences.⁴³ Further refinements of technique may allow their differentiation in the future. Chorionic gonadotropin of normal pregnancy contains a fraction of biologically active hormone and a smaller fraction of biologically inactive, immunologically active hormone. The ratio is reversed in trophoblastic disease,⁴⁴ a fact that could be the basis for a diagnostic test. The primary biologic activity of human chorionic gonadotropin seems to be from luteinizing hormone which, of course, is responsible for the compound lutein cysts seen with trophoblastic tumors. Why these cysts occasionally appear after a mole has been evacuated remains unanswered. Perhaps the pituitary "rebounds" after being suppressed by human chorionic gonadotropin. Molar gonadotropin may have altered activity, because it has been shown that estrogen levels are usually normal in that disease.⁴⁵

Conclusions

The concept of trophoblastic disease is confusing, even to the initiated. To complicate the clinical management, common diagnostic criteria are not shared by investigators. Consequently, evaluation of

Continued

current treatment, especially chemotherapy, is difficult. In the future, new diagnostic tests for the gestational trophoblastic

tumors will evolve, probably from the field of immunology. From that field also, additional modes of treatment probably will be derived.

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References

1. Joint Project for Study of Choriocarcinoma and Hydatidiform Mole in Asia: Geographic Variation in the Occurrence of Hydatidiform Mole and Choriocarcinoma. *Ann N Y Acad Sci* 80: 178, 1959.
2. Moir, J. C.: *Operative Obstetrics*. Ed. 7, Baltimore, Williams & Wilkins Company, 1965, 1003 pp.
3. Acosta-Sison, H.: Changing Attitudes in the Management of Hydatidiform Mole. *Amer J Obstet Gynec* 88:634, 1964.
4. Manahan, C. P., Manuel-Limson, G., and Abad, R.: Experience With Choriocarcinoma in the Philippines. *Ann N Y Acad Sci* 114:875, 1964.
5. Márquez-Monter, H., de la Vega, G. A., Robles, M., and Bolio-Cicero, A.: Epidemiology and Pathology of Hydatidiform Mole in the General Hospital of Mexico: Study of 104 Cases. *Amer J Obstet Gynec* 85:856, 1963.
6. Douglas, G. W.: Discussion. *Ann N Y Acad Sci* 80:195, 1959.
7. Edmonds, H. W.: Genesis of Hydatidiform Mole: Old and New Concepts. *Ann N Y Acad Sci* 80:86, 1959.
8. Husel, D. H.: Six Recurrent Hydatidiform Moles. *Amer J Obstet Gynec* 93:287, 1965.
9. Parsons, L., and Sommers, S. C.: *Gynecology*. Philadelphia, W. B. Saunders Company, 1962, 1250 pp.
10. Harper, W. F., and MacVicar, J.: Hydatidiform Mole and Pregnancy Diagnosed by Sonar. *Brit Med J* 2:1178, 1963.
11. Novak, E. R., and Woodruff, J. D.: *Gynecologic and Obstetric Pathology: With Clinical and Endocrine Relations*. Ed. 5, Philadelphia, W. B. Saunders Company, 1962, 713 pp.
12. Delfs, E.: Chorionic Gonadotropin Determinations in Patients With Hydatidiform Mole and Choriocarcinoma. *Ann N Y Acad Sci* 80:125, 1959.
13. Lee, A. T. C., and Siegel, I.: Hydatidiform Mole With Rupture of the Uterus: Report of a Case. *Obstet Gynec* 26:133, 1965.
14. Brown, E. J., and Effer, S. B.: Induction of Labor in Hydatidiform Mole by Intrauterine Infusion of Hypertonic Glucose Solution. *Amer J Obstet Gynec* 92:1160, 1965.
15. Friedman, N. B.: Discussion. *Ann N Y Acad Sci* 80:149, 1959.

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Gulliver's Travels — Jonathan Swift*

Gulliver on Diseases and Doctors

"It would be endless to give a catalogue of all diseases incident to human bodies; for they could not be fewer than five or six hundred, spread over every limb, and joint: in short, every part, external and intestine, having diseases appropriated to each. To remedy which, there was a sort of people bred up among us, in the profession or pretence of curing the sick . . . Their fundamental is, that all diseases arise from repletion; from whence they conclude, that a great evacuation of the body is necessary, either through the natural passage, or upwards at the mouth . . . But, besides real diseases, we are subject to many that are only imaginary, for which the physicians have invented imaginary cures; these have their several names, and so have the drugs that are proper for them.

"One great excellency in this tribe is their skill at prognosticks, wherein they seldom fail; their predictions in real diseases, when they rise to any degree of malignity, generally portend death, which is always in their power, when recovery is not: and therefore, upon any unexpected signs of amendment, after they have pronounced their sentence, rather than be accused as false prophets, they know how to approve their sagacity to the world by a seasonable dose."

*See *Minnesota Med* 49:1689, 1966.



Clinical Path Conference

Fever, Hemolytic Anemia, and Uremia

THIS 58-year-old white construction worker was first admitted to St. Barnabas Hospital on May 11, 1965, to evaluate his weight loss. He had developed severe diarrhea one year previously and had had several exacerbations with up to six to eight stools a day. His weight had decreased about 25 to 30 pounds during this period, but he had gained 10 pounds after the diarrhea subsided. He had been a known diabetic for six years, maintained on tolbutamide rather than insulin, and had experienced urinary frequency and increased thirst for six months. Although he tested his urine only infrequently, it always showed sugar.

He appeared older than his stated age and had a blood pressure of 170/110 and a normal temperature and pulse. No masses were felt. The lungs and heart were normal; he had reduced reflexes. His blood sugar was 200 mg./100 ml., cholesterol 200 mg./100 ml., and PBI 2.6 mcg. He was treated with insulin and discharged on 25 units, a diabetic diet, and a thyroid preparation.

He was re-admitted two weeks later with chills and night sweats. He had no diarrhea and felt well until his night chills started. Five days before admission, he had become confused, febrile and weak, and had again developed diarrhea. When seen at his local hospital, he had a blood sugar of 300 mg. per cent and was treated with 40 units of insulin. His sensorium fluctuated from clear to confused. Before transfer to Minneapolis his mind was clear, but on arrival he was confused, incontinent, and in a shock-like state.

On examination he was confused and had irregular respiration. The blood pressure was 90/50, and the temperature was 102° F. The examiner could not feel the spleen or liver. The patient's wife said he had worked as a foreman of a construction crew in Africa in April of 1965.

Laboratory data included a hemoglobin of 7.3 Gm. per cent, a wbc. of 9,850, and a differential of 8 polymorphonuclear leukocytes, 42 band forms, 4 myelocytes, 5 monocytes, 38 lymphocytes, and 3 plasma cells. The smear showed 5 normoblasts/100 wbc. The urinary sediment revealed a trace of albumin, 3+ sugar, 2 to 6 hyaline and 6 to 15 granular casts/lpf, and 0 to 2 wbc/hpf. Initially, his urine sediment showed no red cells, but on two later occasions 20-30 RBC/hpf. were seen. The urine was hematest negative. Chemical tests included glucose of 240 mg./100 ml., blood urea nitrogen of 35 mg./100 ml., sodium of 130 mEq/l, a chloride of 98 mEq/l, potassium of 4.2 mEq/l, carbon dioxide combining power of 13 mEq/l, creatine clearance of 25 cc./minute, a protein-bound iodine of 2.6 mcg. and a cholesterol of 200 mg./100 ml. The sequential acid base studies are shown in Figure 1. The urine culture disclosed about 5000 colonies of *Escherichia coli*.

After four to five days the patient began to void 3500 cc. of urine a day. His fever returned, and his hemoglobin fell in spite of eight transfusions. The creatinine clearance two weeks after admission was 25 cc./min. and five days later was 11 cc./min. The BUN at this time was 95 and increased to 120. His urine output varied from 3000 to 3500 cc./day. He was given increased fluid, but he continued to sweat profusely and remained confused. His polyuria subsided and the BUN declined to 45 in six weeks. Then he again became febrile, his hemoglobin fell, and his BUN increased to 65. A fluctuant mass developed in his buttocks, which was incised, yielding *Staphylococcus aureus*. Again he improved and was discharged 10 weeks after admission.

Continued

CLINICAL PATH CONFERENCE

He was re-admitted in late August with chills and slight fever. In the intervening time he had been well, alert, and in good diabetic control. His BUN was 42 and his hemoglobin 11 mg. per cent after transfusions.

He was again re-admitted in October 1965 for recheck and brought in a small firm tissue-like fragment he had passed in his urine, stating that he had passed a similar fragment one week previously but was unable to retrieve it. Culture of urine again revealed *E. coli*. BUN was 39 mg./100 ml., FS 135 mg./ml., and wbc. 13,000.

He was examined for the last time in May, 1966, when he had peripheral edema, had gained ten pounds in weight, and complained of dyspnea. The heart size was increased. Creatinine was 3.4 mg./100 ml.; hemoglobin, 12.1 Gm. per cent; specific gravity of the urine, 1.007. Urine culture was negative and wbc. 10,700. He was given diuretics, improved, and was discharged.

Discussion

Dr. Dennis Kane:*

This 58-year-old white man was first admitted in May, 1965, to evaluate his weight loss. Before that he had had diarrhea for about one year with six to eight stools a day. Did his doctors perform either stool cultures or proctoscopy?

Dr. Wayne A. Chadbourn:** Not so far as we know.

Dr. Kane:

I have to consider bacterial diarrhea or ulcerative colitis in a man with his travel history. A patient who had been to Africa and who has diarrhea should have had a proctoscopy, and his stool should have been studied for ova and parasites. He was denied the benefit of these studies; but we must persevere and continue to follow him as he gets into more trouble.

He then proceeded to lose from 25 to 30 pounds. This is an alarming symptom, particularly when the weight loss is not purposeful. Do we have a baseline weight on him?

Dr. Chadbourn: His weight decreased from 175 pounds to 150 pounds.

Diabetes

Dr. Kane:

A 25-pound weight loss in William Howard Taft would be hardly detectable, but in Calvin Coolidge it would alarm us. Now, let's get the meat of his problems. When the patient was 52, his doctor diagnosed diabetes mellitus, presumably postmaturity-onset diabetes. These diabetics are often overweight and can be maintained on tolbutamides. This patient's diabetes was controlled for six years on such a regimen without insulin.

Then he showed the classic triad of diabetes with polyuria, polydipsia and weight loss. He checked his urines and was constantly spilling sugar, which could mean an alteration of his metabolism of glucose or an exacerbation of his diabetes. The most common cause of the latter is infection, and I assume he had a kidney infection.

When he was examined, he looked older than he was. Premature aging is typical of diabetes. He was hypertensive with a high diastolic pressure which indicates that he had developed trouble in one of the target organs of diabetes — the kidney. Pyelonephritis is an exceedingly common disease in diabetics, and it is a common sequel of longstanding diabetes.

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**Pathologist, St. Barnabas Hospital.

Laboratory Data

At 200 mg./100 ml. the blood sugar was elevated but not startlingly so. Now we come to a paradoxical bit of information. His cholesterol was 200 mg./100 ml., and his PBI (protein bound iodine) was 2.6 mcg. per cent. I have never seen a patient with hypothyroidism with this low a cholesterol. Furthermore, it is unusual indeed for an individual with myxedema to have a serum cholesterol in the low normal range. How can we account for a low cholesterol and low PBI? Mercurial diuretics can lower the PBI, since they precipitate iodine and thus artificially lower the PBI. Did he receive any mercurials?

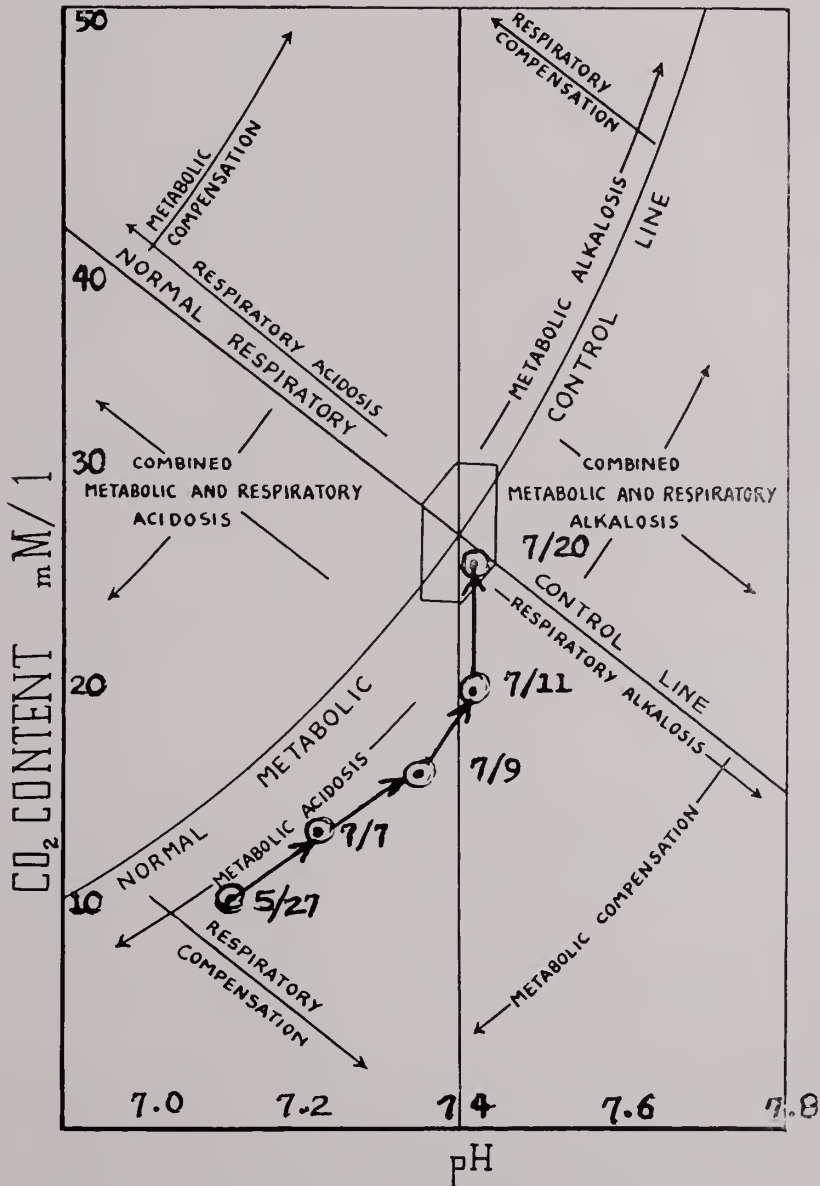


Fig. 1 — A "metabolic map" of the patient's acid-base status. The pH's and CO₂ contents were performed on venous blood. The first determinations indicate metabolic acidosis; later values show a return to normal. The normal region is the central hexagonal area.

Continued

Dr. Chadbourn: He was given no mercurial diuretics.

Dr. Kane:

The nephrotic syndrome reduces the PBI. Here the mechanism for lowering the PBI is related to loss of iodine-carrying compound protein into the urine. Nothing in the protocol indicates that he was spilling protein, and his physicians did not treat him for the nephrotic syndrome.

Discharge and Readmission

His physician treated him with thyroid and insulin and discharged him. He was readmitted two weeks later with chills and night sweats. He had felt well until his night chills started. Five days before admission he had become confused, afebrile and weak and had developed diarrhea again. His chest x-rays showed a rapid onset of pulmonary edema with fluid in the left pleural space.

Congestive heart failure, particularly right heart failure, in a patient with no previous cardiac difficulties deserves comment, but first I will try to explain the chills and fever. This patient had an acute process with chills, night sweats, then confusion. His fever, weakness, and the flare-up of the diarrhea indicate a pansystemic disease.

"Shock-Like" State

He was first seen at his local hospital with a blood sugar of 300 which I interpret as a reaction to infection and indication of increased glycolysis.* He was treated with 40 units of insulin. His diabetes at that particular time was not life-threatening, but he was said to be in a "shock-like" state, which is a euphemism for shock.

This patient was in shock. His blood pressure was 90/50; he was not perfusing his brain; his respirations were irregular; and his temperature was elevated. His neurological examination was normal. He had no localizing signs of pyramidal tract involvement, of cerebral hemorrhage, or of extradural bleeding.

Hemolysis

Now we come either to the crux of the protocol or to a large "red herring." His wife recounts that he worked as a foreman of a construction crew and had had three jobs in Africa in recent years. He was last in Africa one month before he was admitted. Where was he in Africa?

Dr. Chadbourn:

Two of the jobs were in Central-Africa. The last was in Kenya.

Dr. Kane:

Now that we know where he was in Africa, let's look at his laboratory data, some of which is striking. His hemoglobin was 7.3 Gm. per cent, his wbc. was mildly elevated, and his urine culture showed *E-Coli*. In the absence of frank bleeding, this man lost half his red-cell volume. I conclude that he was hemolyzing his red cells. Was a reticulocyte count, fecal urobilinogen, or bone marrow done?

*See Test Your Word Score Page 63.

Dr. Chadbourn:

His reticulocyte count was 4.6%. The other studies were not done.

Dr. Kane:

Hemolytic anemias usually, but not always, have a reticulocyte count much higher than 4.6%. Sometimes pernicious anemia treated with B-12 will respond with a reticulocytosis of similar range as hemolytic process. But he had no stigmata of pernicious anemia, and I think he had hemolysis. His hemolysis was associated with fever. His fever continued, and his hemoglobin kept declining despite blood replacement. Again no mention was made of bleeding.

Renal Failure and Heart Failure

We now go on to find out that he had creatinine clearance two weeks after admission of 25 cc./minute. Five days later it fell to less than half of that. The endogenous creatinine clearance is essentially the same as the inulin clearance. It is a measure of glomerular filtration rate and is usually constant and unaffected by protein metabolism or urine volume.

I suspect a lower nephron nephrosis developed in this patient. His kidneys were probably overloaded with red cells, his tubules may have been plugged with hemoglobin casts, and because of heart failure he was perfusing his renal tissue poorly. He may have gone into hyperkinetic failure because of sudden anemia. Only a limited number of conditions produce hyperkinetic, or high output, or hyperdynamic failure. In this condition a disparity exists between the venous pressure and the circulation time. We see it in shunting diseases like left to right shunts, large pulmonary arteriovenous anastomosis, telangiectatic diseases, and cirrhosis. It occurs in portal cirrhosis when there is a shunting between the systemic and portal circulations. One sees it in Paget's disease* when shunts develop in bone. One sees it in thyrotoxicosis. No venous pressure or circulation time is recorded for this patient.

But the patient had none of these diseases, and the logical cause of his heart failure was severe anemia. Renal failure complicates the interpretation of his anemia. His rapidly mounting nitrogen retention would depress the bone marrow and suppress the synthesis of myeloid and erythroid cells.

Now let us consider his renal failure. His ability to concentrate was lost. According to the protocol his specific gravity was 1.007. His physicians increased his fluid intake to overcome dehydration, but the patient remained confused, and he sweated profusely. This information is important because patients with uremia usually sweat poorly. When you see an ambulatory sallow patient who does not sweat, order a BUN. Frost often develops in these patients in the place of perspiration. I wonder, therefore, if this patient had true azotemia. His clinical course affirms my impression. His BUN came down to 45 in six weeks, and his output increased. In acute renal failure, the BUN may go in a few days from 10 up to 180 mg. per cent. This may occur with incompatible blood transfusion or crush syndrome. When the cause is reversed, the BUN falls as much as 50 mgm./100 ml. per day. Once it reaches about 45 mg./100 ml. it drifts slowly towards normal. When the BUN is in the 40s it can still exert a toxic

*See Page 113.

Continued

influence on the bone marrow, and the patient may continue to have marrow depression. As this patient's BUN came down, his hemoglobin went up. Then his fever returned, his hemoglobin dropped, and his BUN climbed.

I think he was following the pattern of a lower nephron nephrosis, triggered by an overload of hemoglobin from hemolysis. The creatinine is a good index of the tubular efficiency. Usually if you multiply the creatinine by 10, you can get a rough estimate of the BUN. But this rule doesn't hold in this patient, and I can't explain the discrepancy.

What else could have given the picture of lower nephron nephrosis? Hypokalemia can produce tubular lesions with an azotemia, but this patient's serum potassium values, which may not reflect his total body potassium, do not justify the diagnosis of hypokalemic nephropathy.

Diabetes and the Kidney

Diabetes could have contributed to the uremic picture. When he was admitted again in October of 1965, he brought with him a small tissue-like fragment that he passed in his urine and said that he had passed a similar fragment one week before. Renal papillary necrosis is a fairly frequent complication of diabetes, and he may have sloughed off a papilla. Papillary necrosis can lead to uremia with and without acidosis. Radiologists can identify papillary necrosis because they see serrations or irregularities on the pyelogram. This patient probably had a pyelonephritis with focal papillary necrosis.

In May of 1966 he showed peripheral edema. Edema could result from hypoalbuminemia secondary to the Kimmelstiel-Wilson syndrome. But patients with this syndrome frequently present with a heavy proteinuria, and their urinary sediment is filled with hyaline and granular casts and doubly refractile fat bodies. Also, the heavy loss of protein results in a nephrotic syndrome with hypoalbuminemia and hypercholesterolemia. He had neither the blood nor the urine changes, and I will discard the diagnosis of Kimmelstiel-Wilson's disease.

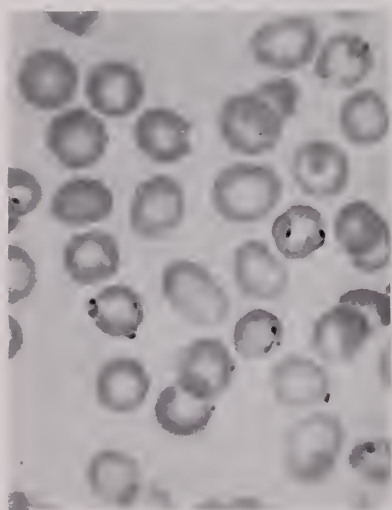


Fig. 2

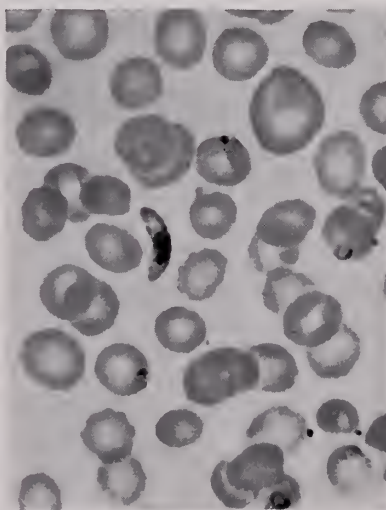


Fig. 3

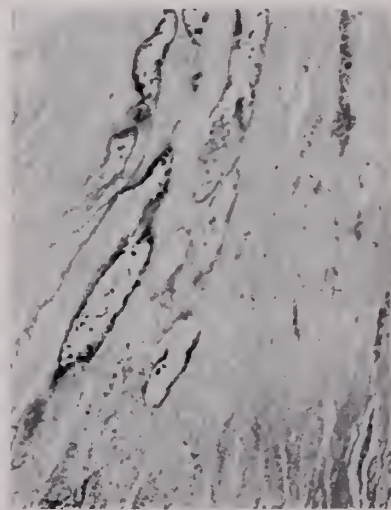


Fig. 4

Fig. 2, 3, and 4 — Figures 2 and 3 are peripheral blood smears showing typical ring forms of *P. falciparum*. Figure 3 also demonstrates a "crescent" form of the parasite. Figure 4 is a high power view (430 $\times$) of the necrotic renal papilla which the patient passed in his urine.

Conclusions

Now it remains to tie this all together in this 58-year-old diabetic with a multi-system disease characterized by fever, hemolysis, and uremia. I can best explain it by going back to Central-Africa. I think that in addition to his diabetes he had a lower nephron necrosis probably caused by hemolysis from *P. Falciparum* malaria. I mention *P. Falciparum* because it has more frequent relapses than malaria caused by other species and is more chronic. It can produce chills, fever, dark urine, and rapidly developing anemia. In conclusion then, I feel this patient with post-maturity-onset diabetes contracted a *Plasmodium Falciparum* malaria; that he then had an *E.-Coli* pyelonephritis; that his malaria recurred associated with massive hemolysis, right heart failure, and lower nephron nephrosis; and that he then had an episode of renal papillary necrosis. One of the penalties for his hospitalization was bilateral staphylococcal abscesses of the buttocks from injections.

Dr. Dennis Kane's Diagnosis

1. *Plasmodium Falciparum* malaria with hemolysis and lower nephron nephrosis.
2. Diabetes mellitus.
3. Pyelonephritis (*E-Coli*) with renal papillary necrosis.

Pathological Diagnosis

Dr. Chadbourn:

Dr. Kane's diagnoses are correct. When this patient was admitted we were alarmed by the massive hemolysis and shock. An overwhelming bacterial infection in hemolysis entered our minds, but we did not think of malaria. However, we quickly made the diagnosis on a peripheral smear. We saw the characteristic ring forms of *P. Falciparum*, or estivoautumnal malaria (Figures 2, 3). His blood showed the effects of hemolysis with nucleated red cells, basophilia, and reticulocytosis. Although he had most of the hallmarks of Blackwater fever — rigor, fever, intravascular hemolysis, collapse, renal failure, and uremia — he never passed black water. Usually these patients have a low nephron nephrosis with necrosis of tubules, hemoglobin casts, and hemoglobinuria. We do not have a kidney biopsy, and I could only speculate on the cause of his uremia. As Dr. Kane predicted, he did pass a necrotic papilla later (Figure 4). Most diabetics with renal papillary necrosis run a fulminating course with uremia and death. We cannot elicit a history of phenacetin ingestion in this patient — the other common cause of papillary necrosis — and we assume he sloughed his papillae because of his diabetes and superimposed pyelonephritis.

Anatomical Diagnosis

1. Estivoautumnal malaria (*P. Falciparum*) with hemolysis.
2. Necrotic renal papillae.

Richard L. Reece, M.D.
Minneapolis, Minnesota

Men usually get somewhere when they develop a brake for the tongue and an accelerator for the brain. — Gas Flame

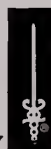


Breast cancer can be highly curable if it is detected early, through regular examinations. Yet, despite all efforts in cancer education and improvements in treatment techniques in the last 30 years,

**THE NUMBER OF
BREAST CANCER DEATHS
PER 100,000 WOMEN
IN THIS COUNTRY
HAS NOT DECLINED.**

While research continues to seek new answers, it is imperative that greater efforts be made to detect breast cancer early and to get women to their doctors when chances of cure are best. That's why the American Cancer Society is encouraging its Divisions across the country to carry out special breast cancer educational programs. Newest of these are demonstration projects in which physicians in a community volunteer one day to giving breast examinations and to teaching hundreds of women breast self-examination. Breast cancer is one of the major cancer problems which we face and which together, doctor, we must try to resolve through intensified research and educational efforts.

AMERICAN CANCER SOCIETY





Grand Rounds

*Thyroid Storm**

JEAN R. ECKERLY, M.D.
Instructor in Medicine

"Let it not be said of the patient with masked hyperthyroidism that it was the physician who wore the mask." — Unknown

Clinical Picture

Thyroid crisis, or "storm," has been defined as a severe exacerbation of hyperthyroidism, characterized by tachycardia, increased pulse pressure, tremor, nausea, vomiting and diarrhea with dehydration, and delirium or coma. However, it is fever which appears to separate "storm" from severe thyrotoxicosis.

The temperature may rise rapidly, and it was once thought that it should reach 103 degrees F. for the diagnosis to be secure.¹ However, a recent report of 21 episodes of thyroid "storm" indicates that a fever of 100 degrees F. or greater is a cardinal sign since it is not seen in uncomplicated thyrotoxicosis.³

Marked tachycardia is characteristic, with pulse rates ranging from 100 to 170 per minute and occasionally greater, but usually around 140 per minute.² The pulse pressure is similar to that seen in thyrotoxicosis, between 60 and 100 mm. mercury. Congestive failure may ensue.

Abdominal pain may be a prominent feature⁴ and, when accompanied by vomiting and diarrhea, is considered an ominous sign.⁵

Probably the most striking feature of "storm" is the appearance of the patient, who may present with a variety of mental and emotional disturbances. These will range from asthenia and coma to extreme restlessness and emotional lability. The tremor may be so marked as to simulate seizure-like activity and will include the face, body and eyes. Patients

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, August 2, 1966.

Continued

in "storm" have been hospitalized on psychiatric wards as hallucinatory schizophrenics.²

Thyroid crisis is most common in patients with Grave's disease,⁴ but a variety of thyroid abnormalities which will produce hyperthyroidism have led to "storm."^{2,6} See Table 1.

The major complication of thyroid storm is death, although acute renal tubular necrosis has been reported.⁷

TABLE 1*
Single Factors Responsible for Thyroid Storm in
8 of 21 Episodes

Single Factor
Pelvic Inflammatory Disease
Appendicitis with Rupture
Bronchopneumonia
SBE
Tooth Extraction
Palpation of Thyroid Gland
Insulin Reaction
Fear

*From Waldstein et al.: Ann Intern Med 52:628, 1960.

Incidence and Mortality

In past years thyroid storm was seen in about 10% of patients who underwent surgery for a toxic goiter⁸ and accounted for 75% of the deaths associated with thyroid surgery.⁹ Mortality from "storm," once 50 to 100%, is still between 20% and 30%.² However, the incidence of storm has dropped so that single cases are now reported in the literature.

Precipitating Factors

"Escape" from iodine preparation and thyroid surgery no longer play an important etiologic role in "storm." It has now become evident that a large variety of stressful situations, such as listed in Table 2, can precipitate storm. Surgical procedures on the unsuspected or mildly hyper-

TABLE 2*
Physical Findings in 21 Episodes of Thyroid Storm

	15 Survivors	6 Fatalities
Temperature, Degrees F.		
100-102.9	7	2
103-106.8	8	4
Heart Rate		
100-139	4	1
140-169	10	3
170-200	1	2
Central Nervous System		
Psychosis	5	1
Coma	2	2
Apathy	2	1
Confusion	5	1
Thyroid Gland		
Type — Nodular	4	1
— Diffuse	11	5
Size — Not Enlarged	0	1
— 2x	8	5
— 3-4x	7	0

*From Waldstein et al.: Ann Intern Med 52:629, 1960.

THYROID STORM

thyroid patient are notable as precipitating events.¹⁰ Because of the difficulty in diagnosis of hyperthyroidism in pregnancy, "storm" occurring at the time of delivery can be a perplexing diagnostic problem.^{11,12}

Pathophysiology

Large amounts of circulating thyroid hormone as the cause of post-thyroidectomy storm seems to be supported by reports of "storm" due to exogenous thyroid poisoning.¹³ However, reports of PBI's and iodine uptakes during storm are not significantly different from those seen in uncomplicated thyrotoxicosis.¹⁴⁻¹⁶ If these cases represent relative thyroid poisoning, then one or more permissive or inhibitive factors must be involved.

There is a large volume of data in support of the theory that epinephrine is responsible for the clinical manifestations of thyrotoxicosis. Hyperthyroid individuals are sensitive to and react more vigorously to the stimulatory effects of catecholamines,^{4,17-19} and the effects of thyroid hormone can be abolished by sympathetic blockade.²⁰ Epinephrine levels have been reported elevated²¹ as well as normal in these patients.¹⁷ Perhaps these observations can be explained by the evidence that hyperthyroids have a decreased ability to catabolize catecholamines, which leads to prolongation of action and accumulation in tissues.²² This, coupled with the observation that thyroxine potentiates the calorogenic effect of epinephrine,²³ has led to the hypothesis that thyroid storm is due to an adrenergic outburst.²⁴ Direct evidence that this is indeed an absolute increase of catecholamines is entirely lacking.

The thyrotoxic patient has also been shown to have rapid clearance of hydrocortisone from the blood,²⁵ and further studies have shown these patients to have relative adrenal insufficiency as defined by a three-day ACTH test.²⁶

Current knowledge about the direct effects of thyroid hormone would place the site of action in the mitochondria where it has been observed to selectively inhibit oxidative phosphorylation,* inhibit certain pyridine nucleotide dehydrogenases, and activate the membrane structure.^{4,27}

Stress, in the relatively adrenal-insufficient hyperthyroid individual, seems to be a factor in the production of thyroid storm, but its exact role is unknown. Storm has been thought of as "decompensated thyrotoxicosis,"⁸ somewhat analogous to ketoacidosis in the diabetic,²⁷ wherein oxidative phosphorylation becomes completely uncoupled and the picture of adrenergic outburst is seen.²⁸ Theoretically, the degree of stress required to produce "storm" should be inversely proportional to the degree of thyrotoxicosis.²⁹

Diagnosis

The diagnosis of storm is made entirely on clinical grounds and usually presents little problem in the known hyperthyroid. Some difficulty may obviously arise in the hyperthyroid with an infection; however, with the knowledge that storm may be precipitated, prophylactic therapy is indicated.

It is the undiscovered or unsuspected hyperthyroid patient who may develop storm under conditions of stress that presents the difficult diag-

*Test Your Word Score Page 63.

Continued

nostic problem. Storm may be confused with infection, CNS disorders and acute enterocolitis. Just how rapidly a patient may develop thyrotoxicosis and progress to storm is unknown, since retrospective analysis of a case may yield subtle clues of hyperthyroidism. However, patients who storm within two months of the onset of their thyroid disease have a very poor prognosis.²

The problem then is when to suspect the presence of hyperthyroidism. Table 3 lists some of the usual findings of the disease and the frequency with which they appear. Any one of the signs of mild hyperthyroidism such as nervousness, diarrhea, muscular weakness and tremor of the hands may be the only clue. The disease should be ruled out in any patient who is being diagnosed as having hypertensive cardiovascular disease, cardiac decompensation, chronic ethanolism,* occult or gastrointestinal cancer, chronic ulcerative colitis, sprue, pheochromocytoma, myasthenia gravis or psychoneurosis. The frequency with which the diagnosis of mild hyperthyroidism is made must necessarily be proportional to the height of the clinician's index of suspicion.

TABLE 3
Incidence of Signs and Symptoms of Thyrotoxicosis

	1*	2**	(Controls)
Symptom			
Nervousness	99	59	21
Hyperhidrosis	91	68	31
Hypersensitivity to Heat	89	73	41
Palpitation	89	75	26
Fatigue	88	80	31
Weight Loss	85	52	2
Dyspnea	75	81	40
Increased Appetite	63	32	2
Hyperdefecation	33		
Diarrhea	23	8	0
Sign			
Tachycardia	100	68	19 (pulse >90)
Goiter	100	87	11
		Diffuse	49
		Nodular	32
		Adenoma	4
Exophthalmos	71	34	2
Lid Lag	71	62	16
Tremor	97	66	26

*1. From Williams Textbook of Endocrinology, Saunders, 1962.

**2. From Means, DeGroot, Stanbury: Thyroid and Its Diseases, McGraw Hill, 1963.

Treatment

The treatment of thyroid storm is aimed at these three known parameters: excess thyroid hormone, increased adrenergic activity, and probable relative adrenal insufficiency.

Iodide, which inhibits the release of thyroxine and tri-iodothyronine from the stored thyroglobulin is given as sodium iodide intravenously in a dose of one to three grams daily^{2,4} or as Lugol's solution 30 to 60 drops daily.

Propylthiouracil, which blocks oxidation of iodide to iodine, is given in a dose of 600 to 1,000 mgm. daily² (methimazole 60 to 100 mgm. daily may be used).

*See Test Your Word Score Page 63.

THYROID STORM

With iodide alone, mortality of 75% or more was still observed. Addition of thioureas* dropped mortality rates to 40% and the addition of reserpine dropped them a bit more.²

Reserpine, given for its sympatholytic effect, is used as a dose of one to three mgm. intramuscularly every six to eight hours to control restlessness and tachycardia (Guanethedine, 20 to 50 mgm. every eight hours may be used).

The most dramatic decrease in mortality is seen with steroid administration and this has now become a routine part of therapy. Usual doses are 40 to 60 mgm. of prednisone or its equivalent daily³⁰ during the period of storm and then rapidly tapered.

This combination of therapy should bring about a dramatic response in two to four days.² The patient should be kept on suppressive therapy until the clinical condition allows definitive treatment.

Prophylactic treatment of the hyperthyroid patient is obviously the most desirable form of therapy.

Case Report

A 50-year-old, white, married female was transferred to this hospital on 6/10/66 with a chief complaint of nausea, shortness of breath, abdominal swelling and lower abdominal discomfort.

She dated her present illness to March, 1966, when she had a 10-day episode of nausea and vomiting unaccompanied by other gastrointestinal symptoms. She was seen by a physician shortly afterward for shortness of breath and ankle swelling. She was given digitalis and diuretics and had a 20-pound weight loss.

On 5/30/66 she was admitted to another hospital with urgency, frequency, and dysuria. Physical examination revealed blood pressure to be 160/70, pulse rate 90 and a large lower abdominal mass. Laboratory data included a BUN of 220 mgm. %, CO₂ 10 mEq/l, chloride 79 mEq/l, potassium 4.6 mEq/l, sodium 129 mEq/l and hemoglobin 8.5 gm. %. Retrograde pyelography revealed bilateral ureterectasis. Ureteral catheterization produced a good urine output and she was transferred to Hennepin County General Hospital for definitive treatment.

Physical examination on admission to Hennepin County General Hospital revealed an ill-appearing woman who was moderately short of breath. Blood pressure was 180/90, pulse rate 88, temperature 98.6 degrees. Positive physical findings were palpable thyroid with a 1 to 2-cm. nodule in the midline (re-evaluation shows this to be a multinodular thyroid, right lobe, larger than the left, estimated at 40 grams). Aortic systolic ejection murmur, nodular tumor mass in the pelvis and moderate peripheral edema were present.

Laboratory data revealed hemoglobin to be 7.1 gm.%, wbc. 11,200 with 95% PMN's, urinalysis 175 to 200 RBC/NPF (ureteral catheters in place), 3+ albumin, 3+ sugar; VDRL negative; ESR 109; BUN 147, creatinine 7.5, calcium 10.4, PO₄ 7.6, Na 131, K 5.6, CO₂ 11, chloride 114 and FBS 121 mgm. %.

Hospital Course: The patient was put into electrolyte balance by peritoneal dialysis, and exploratory laparotomy was performed on the fourth hospital day. A large myomatous uterus was removed. Following surgery urine output improved markedly. However, immediately postoperatively the patient was noted to be febrile (T. 102.4 degrees) with a pulse of 108 and blood pressure 170/70, and she remained moderately febrile with a tachycardia of around 110/min. until the fourth postoperative day when she was noted to have rapid eye movements, marked twitching of extremities and mental confusion. She remained confused and on the sixth postoperative day developed a fever of 103 degrees F., with pulse 120, accompanied by diarrhea. Blood cultures, spinal fluid, sputum and stool cultures were negative. Proteus was found in the urine and the patient was treated with chloromycetin and vancomycin with little clinical response. Hypocalcemia and hypomagnesemia were suspected and treated, but laboratory values failed to support these diagnoses and the patient's condition remained unchanged. On the eighth postoperative day she was started on Solucortef, 300 mgm/day, Na iodide, 1.5 gm/day, propylthiouracil, 800 mgm/day, and reserpine, 1.5 mgm. I.M. q. 6 hours. Within four days the pulse rate was down to 80 per minute and the

*See Test Your Word Score Page 63.

Continued

GRAND ROUNDS

temperature normal. ET-3 on the day therapy was instituted was 20.6%. Total thyroxine drawn after the patient had responded to therapy was 5.58%.

The patient is currently under control with propylthiouracil which is being tapered to allow thyroid function studies to be done. She has continued to show evidence of renal failure requiring dialysis, which has been done without incident.

Diagnoses: 1. Renal failure secondary to obstructive uropathy from myomatous uterus.

2. Thyroid storm secondary to toxic nodular goiter.

References

1. Rives, J. D. and R. M. Shepard: *Amer Surg* 17:406, 1951.
2. Waldstein, S. S., S. J. Slodki, G. I. Kaganiec and D. Bronsky: *Ann Intern Med* 52:626, 1960.
3. Lahey, F. H.: *New Engl J Med* 199:255, 1928.
4. Means, J. H., L. J. DeGroot, J. B. Stanbury: *The Thyroid and Its Diseases*. McGraw Hill, New York, 1963.
5. Rawson, R. W., M. Sonenberg and W. L. Money: *Diseases of Metabolism*, p. 1159, W. B. Saunders, Philadelphia, London, 1964.
6. Bloise, W., W. Nicolau, B. L. Wajchenberg, R. R. Pieroni, A. C. Toledo, E. Mattar and A. B. de Ulhoa Centra: *J Clin Endocr* 23:1096, 1963.
7. Lamberg, B. A. et al.: *Acta Med Scand* 175:325, 1964.
8. McArthur, J. W., R. W. Rawson, J. H. Means and O. Cope: *JAMA* 134:868, 1947.
9. Thompson, N. W. and W. J. Fry: *Arch Surg* 89:572, 1964.
10. Lounsbery, F., J. M. Lebowitz and M. E. Anderson: *Quart Bull Northwest Univ Med Sch* 36:341, 1962.
11. Kamm, M. L., J. C. Weaver, E. P. Page and C. C. Chappell: *Obstet Gynec* 21:460, 1963.
12. Quenter, K. E. and G. A. Friedland: *Obstet Gynec* 26:403, 1965.
13. Schottstardt, E. S. and M. Smoller: *Ann Intern Med* 64:847, 1966.
- 14-30 May be secured from the Grand Rounds Editor.

Speaking of Operations

Until I passed through the experience of being operated on myself, I never really realized what a precious conversational boon the subject is, and how great a part it plays in our intercourse with our fellow beings on this planet. To the teller it is enormously interesting, for he is not only the hero of the tale but the rest of the cast and the stage setting as well — the whole show, as they say; and if the listener has had a similar experience — and who is there among us in these days that has not taken a nap 'neath the shade of the old ether cone? — it acquires a double value. "Speaking of operations —" you say, just like that, even though nobody present has spoken of them; and then you are off, with your new acquaintance sitting on the edge of his chair, or hers as the case may be and so frequently is, with hands clutched in polite but painful restraint, gills working up and down with impatience, eyes brightened with desire, tongue hung in the middle, waiting for you to pause to catch your breath, so that he or she may break in with a few personal recollections along the same line. From a mere conversation it resolves itself into a symptom symposium, and a perfectly splendid time is had by all. — Irvin S. Cobb: *Speaking of Operations*.

A Religious Practice

If you have operated conscientiously on the rich for a proper fee and on the poor for charity, you need not play the monk, nor make pilgrimages for your soul. — Henri de Mondeville (c. 1260-1320)

Lacerations of Hand Tendons

Current Concepts of Treatment

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ALTHOUGH LOWEST on the scale of tissue priorities, tendon injuries challenge surgical judgment and skill as much as if not more than do injuries of any other tissue. To join the ends of a severed tendon by surgical suture is easy, but to obtain a normal gliding structure is difficult.

Anatomic Considerations

In most areas of the hand, the tendon is surrounded by paratenon which is areolar tissue filling the interstices of the fascial compartment in which the tendon is situated. Some tendons, in certain sites where they might rub against bone or other friction-generating surfaces, are enclosed in sheaths. Embryologically this sheath is the invagination of a mesenchymal cleft which has undergone synovial differentiation during the second month of fetal life. For practical purposes, this invagination produces two sheaths. The outer one is a connective tissue tube, called the "fibrous" or "parietal sheath," with its exterior attached to the structures that surround it. The inner, visceral sheath directly encloses the tendon, is firmly attached to it, and is called the "epitenon." The mesenterylike double fold of synovial membrane connecting the two sheaths is called the "mesotenon." The space between the epitenon and the fibrous sheath contains synovial fluid which is an excellent lubricant.

Preservation of blood supply to the tendons comprises the key to the management of tendon injuries.¹ Despite the extremely

low metabolic requirements and extremely low respiratory rate of tendon, its survival depends on an adequate blood supply, rather than on diffusion of gases and nutrients from surrounding tissues. In the hand, specific architectural needs of different areas modify the blood supply. Tendons with paratenon receive blood vessels from all sides and therefore heal rapidly. Those tendons invested in sheaths derive their blood supply from the mesotenon, all branches originating in the bed deep to the tendon. From this bed they pass into the mesotenon, branch into arcades of vessels, and enter the tendon. Each arcade has some anastomotic connection with the ones lying on either side of it, but primarily it nourishes a small localized segment of tendon. Blood supply to any single segment will not support circulation in adjacent segments more than 1 or 2 cm. long; as a result, large portions of any tendon freed at operation must function as free tendon grafts until a blood supply is restored by the ingrowth of vessels. In the finger this mesotenon is reduced to two vincula, the longus and the brevis, carrying the vessels (Figure 1).

In the hand, tendon sheaths extend proximally from the insertion of the flexor superficialis on the middle phalanx to their termination at a level just proximal to the metacarpophalangeal joints in the palm. Externally this area is from the middle of the middle phalanx proximally to the distal palmar crease. The flexor sheath of the thumb extends from the terminal phalanx to a point 2 or 3 cm. superior to the proximal volar crease of the wrist. Wherever a

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tendon spans the concavity of a joint, a pulley mechanism is necessary to prevent "bowstringing." These pulleys, the annular ligaments, are thickened, tough parts of the fibrous sheath and are between joints, not opposite them.

Tendon Healing

Tendons are not inert structures, even though their metabolism is low, and they respond to physiologic stress by hypertrophy. Disuse results in atrophy and degeneration. When lacerated, tendon ends become edematous and proliferate. If not coapted* exactly, these ends adhere to surrounding injured tissue, a tendency which makes it essential not only that the ends be carefully coapted but that no unopposed fibers are left free. Many techniques of tendon suture have been devised. The site of repair should be kept well away from the skin incision if possible.

Suture Material and Technique

Catgut is unsatisfactory for tendon suture because of the possibility of infection after tissue rejection. Silk occasionally causes a reaction, although modern, untreated silk is less likely to do so. Stainless steel wire provokes the least reaction; it glides easily and is strong for its diameter. Kinks in the wire weaken it and should be avoided. Monofilament, 34-gauge wire is apparently the most popular for tendon-to-bone suture, while multistrand wire is gaining in popularity for tendon-to-tendon suture. Monofilament wire can be placed in such a way

that it can be removed when tendon healing is complete (Figure 2-a). This is particularly important where tendons glide in sheaths or lie near a joint or just beneath the skin.

Further exposure of the tendon to be sutured may be necessary. Additional incisions should be made without crossing flexion creases at a right angle. Less exposure is needed distally than proximally since there is no muscle pull on the distal tendon ends and since passive flexion of the fingers will deliver the distal ends into the wound.

In suturing tendons, handling should be delicate, to minimize reaction and scarring as much as possible. The tendon ends must be accurately opposed and the gliding surface must be free of blemish. All crushed parts should be removed after the sutures are secured.

Repair of Extensor Tendons

Extensor tendons of the hand can usually be repaired primarily at almost any level in clean incised wounds if skin coverage is adequate^{3,4} (Figure 3). The paratenon of extensor tendons ensures a good blood supply for healing. Even without suture the extensor tendons often unite with bridges of scar tissue and, because they are surrounded by the loose areolar tissue, are able to glide and function satisfactorily.

In contrast to flexor tendons, excursions of the extensors are shorter and their motions are weaker, placing less stress at the repair site. However, certain anatomic features call for great care and exacting tech-

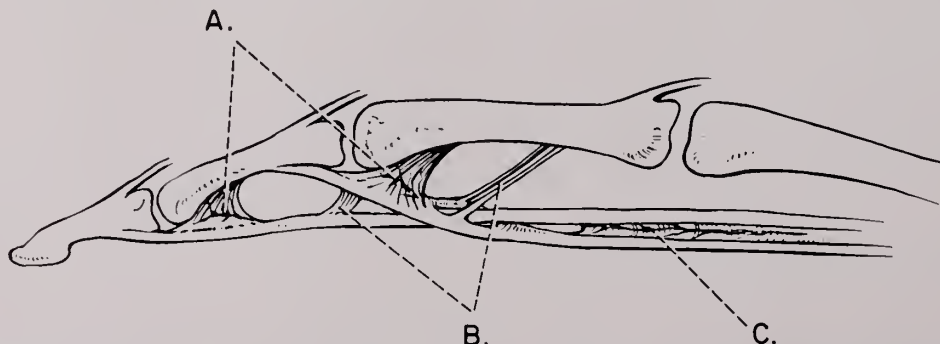


Fig. 1 — Blood supply to tendons in digital sheath. (A) = vincula brevis; (B) = vincula longus; and (C) = mesotenon connecting superficialis and profundus. (Modified from Smith, J. W.: Blood Supply of Tendons. *Amer J Surg* 109:272, 1965.)¹

*See Test Your Word Score Page 63.

nique in repair or replacement. Extensor tendons in the fingers and thumb are extremely thin, form a part of the joint capsule, and lie in close proximity to bone and skin. The complex relationship existing be-

tween extensor tendons and the intrinsic mechanism must be preserved.^{3,5,7}

Mallet Finger

Primary repair is indicated in lacerations

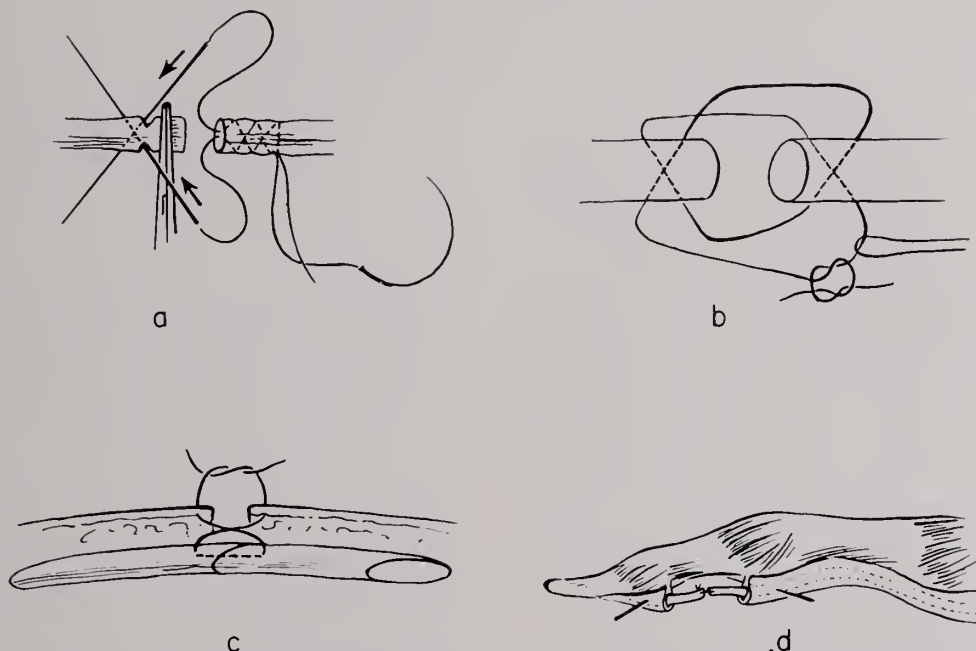


Fig. 2 — Common suture techniques. (a) Bunnell pullout suture; (b) double right-angle suture; (c) figure-of-eight suture; (d) Verdan's transfixion technique. (Modified from Peacock, E. E., Jr.: *Practical Joints in Repair of Injured Tendons*. Hosp Med October, 1965, p. 28.)²

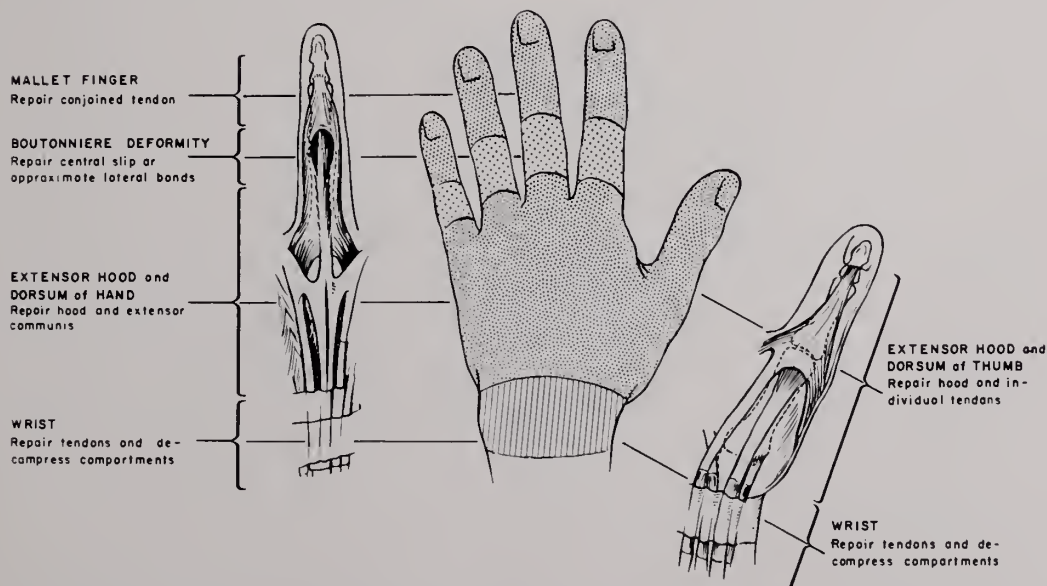


Fig. 3 — Extensor tendon repair. (Modified from Holm, C. L., and Embick, R. P.: *Anatomical Considerations in the Primary Treatment of Tendon Injuries of the Hand*. J Bone Joint Surg 41-A:599, 1959;⁵ Kelly, A. P., Jr.: *Primary Tendon Repairs: A Study of 789 Consecutive Tendon Severances*. J Bone Joint Surg 41-A:581, 1959.⁶)

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of the conjoined tendon. Immobilization in extension is most satisfactorily obtained with a Kirschner wire across the distal joint or with a plastic or aluminum splint. Severe, untreated mallet-finger deformity may lead to hyperextension of the proximal interphalangeal joint because of unopposed pull of the central slip.

Boutonnière Deformity

Lacerations in the region of the middle joint may involve the extensor slip to the middle phalanx, causing a so-called button-hole or boutonnière deformity which may not be immediately recognizable. This deformity consists of flexion of the middle joint and extension of the distal joint because of volar displacement of the lateral bands. Therefore, this particular region should be carefully explored during primary wound repair and the central slip restored if possible. Failing this, the lateral bands should be approximated on the dorsum of the finger and sutured together to prevent volar displacement. Immobilization of the finger in extension is required.

Extensor Hood and Dorsum of Hand

Injuries to the extensor hood, including

the lateral expansions with intrinsic insertions, must be carefully sutured. The long extensor tendons interdigitate freely over the dorsum of the hand. This prevents retraction, and primary repair is readily accomplished by coaptation and appropriate splinting with the wrist in extension. A single figure-of-eight wire passed through the skin and the tendon approximates the tendon ends (Figure 2-c). Splinting in extension relieves the tension on the suture line; these tendons do not retract far when cut.⁸

Wrist

At the wrist, the extensor tendons are grouped in six compartments under the dorsal carpal ligament, each with a separate tendon sheath. When cut, they retract into the forearm. Primary repair is anatomically more difficult in this area, as it must be accompanied by resection of the mucous sheaths and decompression of the compartments by longitudinal incision of the dorsal carpal ligament.⁵ When all tendons are divided, repair of every one should not be attempted. Primary consideration must be given to providing good extension of the wrist and abduction of the thumb; extension of

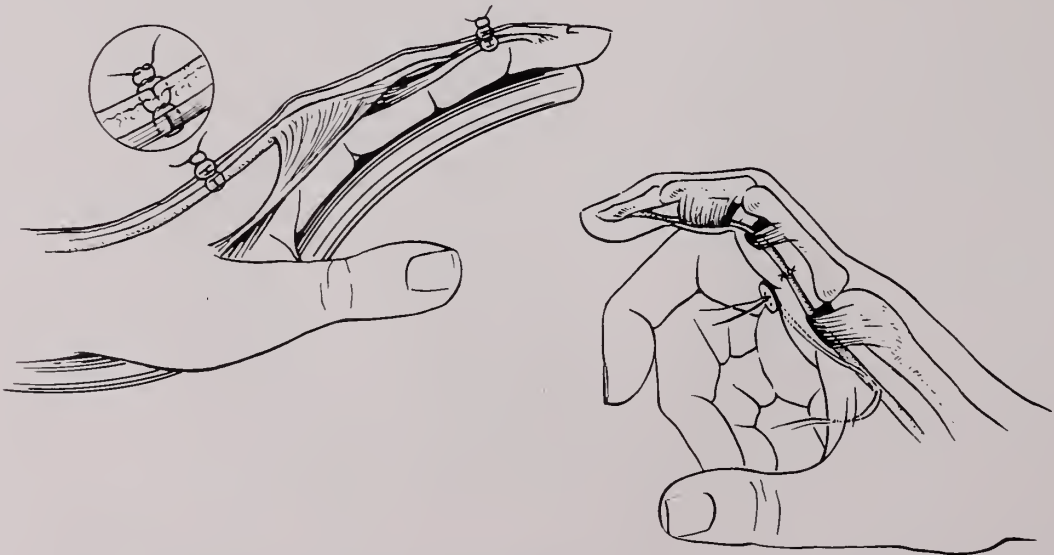


Fig. 4 — Applied techniques. *Left*, For primary or secondary suture, figure-of-eight stitch approximates the tendon ends. Splinting prevents tendon ends from being pulled apart. *Right*, Suture-at-a-distance reduces tension on tendon repair. Note excision of sheath overlying repair. (Modified from Boyes, J. H.: *Bunnell's Surgery of the Hand*. Ed. 4, Philadelphia, J. B. Lippincott Company, 1964, 791 pp.)⁸

the fingers and thumb is secondary. The extensor carpi radialis brevis muscle is the most important wrist extensor, and the abductor pollicis longus is the most important tendon on the dorsoradial aspect of the thumb; these should be repaired. Finger and thumb extension can be restored later or given a mass extension action by providing one or two motors to power the extension.⁹

Thumb Extensor Tendons

All lacerations of the thumb extensor mechanism may be repaired primarily and splinted in extension.

When the long extensor tendon is cut over the base of the thumb, it retracts considerably and, because of its angulated position around Lister's tubercle of the radius, repair is more difficult. Primary repair may require that the tendon be rerouted subcutaneously to permit approximation of the ends without tension.

Primary repair of the extensor pollicis brevis tendon, which functions as both extensor and abductor, is desirable but not always essential if the long extensor and abductor tendons are intact. Isolated lacerations of the extensor pollicis brevis tendon cause little deformity and may not be diagnosed. Failure to repair it, however, can result in incomplete extension of the proximal

phalanx and slight imbalance of the hood mechanism.

Repair of the abductor pollicis longus tendon is essential because this musculotendinous unit functions not only as an abductor but also as a stabilizer of the important metacarpomultangular articulation of the thumb. It presents no particular anatomic difficulty in primary repair.⁵

In general, extensor tendon repairs are more satisfactory in the thumb than in the fingers.⁶

Splinting

In all extensor tendon injuries, the wrist should be extended, and the metacarpophalangeal joints should be maintained in slight flexion during the period of immobilization (Figure 4-left). This avoids contractures and imbalance associated with prolonged hyperextension. Splinting is mandatory for at least three weeks, and some protection against the pull of the powerful flexors should be maintained by keeping the wrist splinted for an additional two weeks.³

Flexor Tendon Repair

Whereas extensor tendons are more commonly injured in the nondominant hand, there is a definite tendency for flexor-tendon

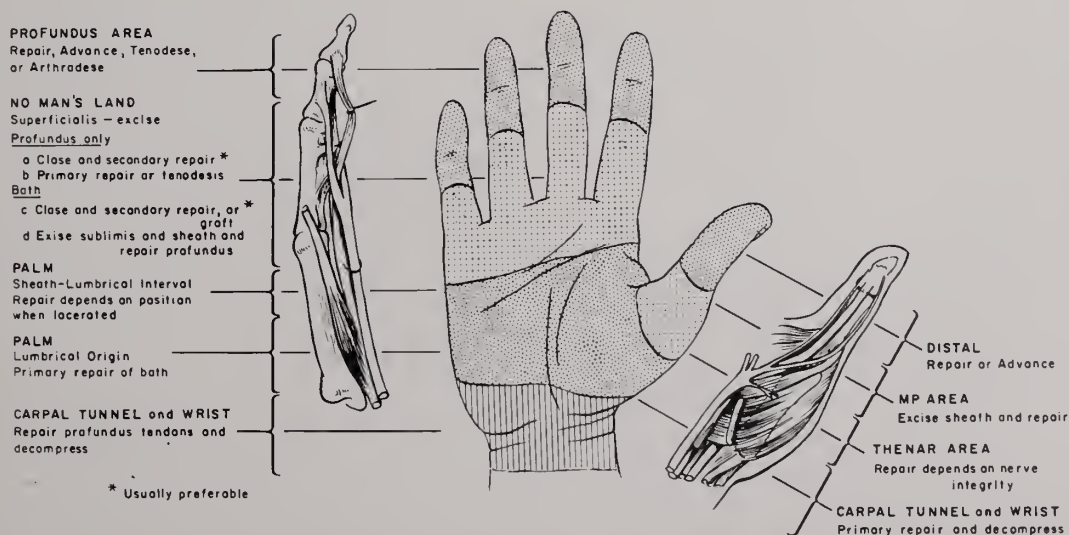


Fig. 5 — Flexor tendon repair. (Modified from Holm, C. L., and Embick, R. P.: Anatomical Considerations in the Primary Treatment of Tendon Injuries of the Hand. *J Bone Joint Surg* 41-A:599, 1959;⁵ Kelly, A. P., Jr.: Primary Tendon Repairs: A Study of 789 Consecutive Tendon Severances. *J Bone Joint Surg* 41-A:581, 1959.)⁶

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injury to occur in the dominant hand. In addition, results of tendon repair are much less satisfactory for flexor than for extensor tendons.⁶ In general, therefore, flexor-tendon injuries are more disabling than are extensor injuries.

Wrist

Primary repair of flexor tendons in the wrist is essential and is anatomically practical because the synovial sheaths or bursae terminate in the wrist and blend with the vascular paratenon (Figure 5). Also, the rich blood supply from the musculotendinous junction facilitates primary repair.^{4,5} However, if all 12 tendons and both ulnar and median nerves were sutured at one level, a great, homogeneous mass of scar tissue might result with no functional activity of any tendon or nerve. In such an event the digital superficialis tendons and wrist flexors are of secondary importance and need not be repaired.^{3,4,9} The wrist flexor tendons are in paratenon and will usually repair themselves in a functional manner.⁹ Since speed of repair and utilization of a minimal amount of suture material are often desirable in multiple profundus-tendon anastomoses in one area, the double right-angle suture is frequently used (Figure 2-b).

*Carpal Tunnel**

A laceration extending entirely through the carpal tunnel would sever nine tendons and the median nerve, a situation which makes repair difficult. The median nerve should be repaired initially and, because of excessive retraction of the tendon ends at this level, primary repair of the profundus and flexor pollicis longus should be attempted. The superficialis tendons should be excised as far proximally and distally as possible through the operative wound. They may be sutured only if the suture lines will lie more proximally.⁴ The ulnar bursa, which envelops the profundus from the ulnar side, should be resected or wrapped about the tendon junctures in an attempt to prevent adherence of individual tendon anastomoses to

each other and to surrounding soft tissues. The carpal tunnel should be completely decompressed by incising or excising the transverse carpal ligament. If possible, the junction of the tendon ends should not be placed within the carpal tunnel; this can be avoided by proper positioning of the wrist.^{5,6,8} The double right-angle suture is again used to good advantage.

Palm

Area of Lumbrical Origin on the Profundus.—When the superficialis and the profundus tendons are lacerated in this area, primary repair of both tendons is feasible because the lumbrical muscle can be interposed between them to prevent cross union. The lumbrical muscle should be interposed with minimal suturing to avoid damage to its nerve supply and to avoid limiting its action.³⁻⁵

SHEATH-LUMBRICAL MUSCLE INTERVAL

When only the superficialis tendon is lacerated, it need not be repaired because there will be little loss of function. When both tendons are lacerated in this region, the repair will be influenced by the position of the fingers at the time of injury. Thus, in lacerations through the distal palmar crease with the hand in extension, primary repair of only the profundus is advisable, as no barrier to cross union with the superficialis exists at this level. The superficialis should be excised. If the tendons are lacerated in flexion, the distal ends will move into the fibrous sheath of the fingers when the fingers are extended. In this case it would probably be most prudent to close the skin and perform a secondary graft, because the junction of the tendon ends would lie within the tendon sheaths distal to the metacarpophalangeal joint.⁵

"No-Man's-Land"

This is the critical and complex area of pulleys extending from the insertion of the superficialis tendon on the middle phalanx proximally to the termination of the flexor sheath in the palm.

In the past the standard treatment has been wound decontamination, skin closure,

*See Yamaguchi, D. M. et al.: Carpal Tunnel Syndrome. *Minnesota Med* 48:22, 1965.

and tendon graft at a later date. In the recent literature there are more and more reports of primary repair, but the variety of techniques indicate that there is no conformity or universally good method. Some authors state that injury within the digital sheath can never be repaired with uniformly good results, whether primary repair or late resection and grafting procedures are used.⁴

Important factors in making a decision between primary repair and secondary repair include the surgeon's knowledge, experience, and skill in the management of difficult tendon injuries, the location of transection, the digit involved, the type of injury and associated injuries, the degree of contamination, the age and occupation of the patient, and the available equipment and facilities, including adequate assistance and postoperative management.^{4,6,8,10}

Those who favor wound closure without primary tendon repair^{4,5,8,11-13} believe that, when the superficialis alone is divided, it should be excised. Early motion will maintain profundus excursion and ensure a functioning finger, with no further treatment necessary. When the profundus alone is divided, it should not be sutured, and the superficialis should not be sacrificed but rather strengthened by early motion (Figure 5). Tenodesis of the distal joint could be done primarily or at a later date. Or arthrodesis of the distal joint could be done later; this is indicated particularly for laborers or those who desire a quick, certain result. In an exceptional case, a thin palmaris or plantaris graft could be used secondarily to restore profundus action. Some authors advocate tendon grafts for index and long fingers because they gain pinch. In musicians and skilled technicians, attempts at tendon grafting for all fingers may be warranted. If both superficialis and profundus tendons are divided, neither should be sutured, and tendon grafts should be inserted later (Figure 5). Usually two to three weeks later, the superficialis is excised and a tendon graft replaces the profundus tendon from its distal attachment to

the proximal half of the palm or well into the area of the origin of the lumbrical muscle.

If results are unsatisfactory, tenolysis* may be done but should be delayed at least six weeks to obtain maximal range of motion and to avoid spontaneous rupture of the graft.

Those who favor primary repair^{3,4,10,14-16} of tendons in no-man's-land agree that, when only the superficialis is divided, primary repair is certainly not indicated. Isolated lacerations of the profundus tendon are rare (Figure 5). Primary repair usually results in adhesions to the sublimis tendon. Excision of an intact sublimis tendon in order to facilitate primary repair of the profundus tendon is mentioned only to be condemned. Any primary procedure should be limited to tenodesis of the distal portion of the tendon to the middle phalanx. This then is similar to what is recommended by those who favor wound closure and secondary repair. The real point of contention is what should be done when both tendons are divided (Figure 5). This is a frequent location for tendon injury, and temptation to carry out primary suturing is great.

All who advocate primary suturing insist on "ideal conditions." These include a clean hand at the time of injury, minimal contamination, laceration by a thin, sharp agent, operation within six to eight hours of injury, an incised wound with no crushing or avulsion, adequate facilities and instruments, trained assistants, and experienced surgeons. These advocates point out that any surgeon who is trained to perform a successful graft of the flexor tendons is also capable of performing a successful primary repair. This might well be our guideline. Thus, anyone not capable of tendon grafting should probably not do primary repair. When experience is limited, treatment should be more conservative.

Most who recommend primary repair believe that the superficialis tendon should be excised. The overlying sheath and the pulley structure at the level of the suture must be excised (Figure 4-right). This allows

*See Test Your Word Score Page 63.

good blood supply at the site of repair and ensures that any future scar at the site of suture will slide freely in both directions without contacting the sheath. The remaining sheath suffices to prevent dislocation of the tendon. The profundus should be sutured accurately with fine epitendinous stitches. Tension on this anastomosis may be reduced by the "suture at a distance" technique (Figure 4-right). Verdan¹⁵ advocates fixing each tendon end with a transverse stainless steel pin to prevent tension (Figure 2-d).

Should adhesions hinder gliding, secondary tenolysis often produces functional results better than those of tendon grafts. For multiple simultaneous flexor cuts on several fingers, primary repair may be more justified than for one cut alone. Also, after primary repair, grafting at a later date is still possible but is more difficult than when the wound only has been sutured.

Distal Profundus Area

This area extends from the insertion of the profundus tendon on the distal phalanx to the insertion of the superficialis tendon midway on the shaft of the middle phalanx. Lacerations here involve only the profundus tendon, making primary repair possible. Excessive retraction of the proximal end is prevented by the vincula. Four possibilities exist.^{4-6,10-12}

1. If the laceration is at least 1 cm. proximal to its insertion, both ends of the tendon can probably be found in the wound, and direct approximation with a pullout suture should be easy. The pulley and the sheath in the vicinity of the junction must be excised.

2. If the distal stump is less than 1 cm. long or is frayed or avulsed, the proximal tendon end can be advanced and fixed directly to the distal phalanx. Several techniques are available, including direct suture or burying the tendon end beneath a small osteoperiosteal hole drilled through the phalanx. The junction should be well distal to the interphalangeal joint, thereby avoiding adhesions in the region of the joint and volar plate. Advancement is limited to 1 or

2 cm. if a flexion contracture is to be avoided. Profundus lengthening procedures in the wrist are not practical. If primary suture is not advisable, a secondary repair may be considered if division has been close to the insertion.¹²

3. If the proximal end has retracted into the palm due to muscle pull, the vincula have ruptured; then it is technically difficult to rethread the profundus tendon down its proper channel through the sublimis bifurcation without inflicting further trauma. In most cases it is better to suture the distal tendon end to the middle phalanx with the distal joint in flexion and the fingertip in pinching position.^{4,5,7}

4. If all else fails, arthrodesis of the distal joint in slight flexion leaves little functional disability.^{5,6,8}

Thumb Flexors

The results of flexor repairs are usually more satisfactory in the thumb than in other digits.⁶ The flexor pollicis longus has no vincula and is without a lumbrical muscle; it lies in the carpal tunnel within its own sheath, and its muscle is independent of the finger flexors. Thus the anatomy facilitates tendon advancement or lengthening during primary repair of lacerations.⁵

Distally, the phalangeal portion of the tendon can be repaired primarily, as in the fingers, by the advancement procedure.⁵

In the metacarpophalangeal joint area, direct suture with resection of the sheath is preferred and can be assisted by tendon advancement or tendon lengthening at the wrist if necessary.⁵

In the thenar area, primary tendon repair is possible but, because of hemorrhage and the presence of overlying digital and motor branches of the median nerve, the surgical approach is often difficult. If the nerve is also severed, then both tendon and nerve should be repaired. If the nerve is intact, simple closure of the wound would avoid further damage. Secondary repair by grafting or transfer of the ring finger superficialis tendon is practicable.^{5,10}

In the carpal tunnel and wrist, the thumb flexor tendon is well situated for primary

repair. The sheath must be resected and the tunnel decompressed.⁵

The long thumb flexor acts primarily on the distal phalanx. Therefore, if the long flexor tendon cannot be repaired, arthrodesis of the interphalangeal joint in slight flexion will restore a useful thumb if the thenar motors are intact.

Splinting

In general, when flexor tendons have been sutured, immobilization — with the wrist in flexion, the involved finger in the position of function, and the other fingers extended — is necessary for three weeks; then, active exercises are begun. Exercises against moderate resistance are begun during the fifth postoperative week.

Secondary Repair

Secondary reconstruction of tendons does not always imply tendon grafting. The most conservative operation which gives the best chance of good function with the least risk should be used. Other operative procedures which may be used include delayed suture, tendon advancement, tendon lengthening,

tendon transfer, tenodesis, and arthrodesis. Experimental work on artificial tendons has been in progress for some time and may provide an additional method of treatment for special cases in the future.¹⁷

Summary

A résumé of current concepts in treating lacerations of tendons of the hand has been compiled from the recent literature, supplemented by practical experience. Anatomic considerations have been stressed because these are the basis for treatment. The choice between primary repair and wound closure with secondary repair of a lacerated tendon of the hand is based on experience. Consistently good results from primary repair of flexor tendons in "no-man's-land" are not easily obtained by surgeons who see these injuries infrequently. Physicians not capable of performing secondary repairs — for example, tendon grafting procedures — are probably not qualified to do primary repairs. When experience is limited, treatment should be conservative. One rarely can be criticized for cleansing and closing the wound and seeing that the patient is given adequate follow-up care.

References

1. Smith, J. W.: Blood Supply of Tendons. *Amer J Surg* 109:272, 1965.
2. Peacock, E. E., Jr.: Practical Points in Repair of Injured Tendons. *Hosp Med* p. 28, 1965.
3. Milford, L.: The Hand. In Crenshaw, A. H.: *Campbell's Operative Orthopaedics*. Ed. 4, St. Louis, C. V. Mosby Company, p. 139, 1963.
4. Swanson, A. B., Flynn, J. E., Chase, R. A., and Boyes, J. H.: M.D.'s Debate Primary Tendon Repair of the Hand. *Med Tribune*. 6:7, 1965.
5. Holm, C. L., and Embick, R. P.: Anatomical Considerations in the Primary Treatment of Tendon Injuries of the Hand. *J Bone Joint Surg* 41-A:599, 1959.
6. Kelly, A. P., Jr.: Primary Tendon Repairs: A Study of 789 Consecutive Tendon Severances. *J Bone Joint Surg* 41-A:581, 1959.
7. Entin, M. A.: Repair of Extensor Mechanism of Hand. *Surg Clin N Amer* 40:275, 1960.
8. Boyes, J. H.: *Bunnell's Surgery of the Hand*. Ed. 4, Philadelphia, J. B. Lippincott Company, p. 791, 1964.
9. Fowler, S. B.: The Management of Tendon Injuries. *J Bone Joint Surg* 41-A:579, 1959.
10. Mason, M. L.: Primary Tendon Repair. *J Bone Joint Surg* 41-A:575, 1959.
11. Peacock, E. E., Jr., and Hartrampf, C. R.: The Repair of Flexor Tendons in the Hand. *Int Abstr Surg* 113:411, 1961.
12. Pulvertaft, R. G.: The Treatment of Profundus Division by Free Tendon Graft. *J Bone Joint Surg* 42-A:1363, 1960.
13. Wakefield, A. R.: The Management of Flexor Tendon Injuries. *Surg Clin N Amer* 40:267, 1960.
14. Lindsay, W. K., and McDougall, E. P.: Direct Digital Tendon Repair. *Plast Reconstr Surg* 26:613, 1960.
15. Verdan, C. E.: Primary Repair of Flexor Tendons. *J Bone Joint Surg* 42-A:647, 1960.
16. Young, R. E. S., and Harmon, J. M.: Repair of Tendon Injuries of the Hand. *Ann Surg* 151:562, 1960.
17. Hunter, J.: Artificial Tendons: Early Development and Application. *Amer J Surg* 109:325, 1965.

An open mind is all very well in its way, but it ought not to be so open that there is no keeping anything in or out of it. It should be capable of shutting its doors sometimes, or it may be found a little draughty. — Samuel Butler

ANNOUNCING
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Gleanings from the Meetings

Minnesota State Obstetrical and Gynecological Society Meeting*

Rochester, Minnesota — April 23, 1966

Well, here we are. We have finished the formal presentation. The entire subject of therapeutic abortion is now open for discussion from the floor.

Obviously, Minnesota is not typical of the nation as a whole. We have less than one per cent Negroes, we have far less than the usual number of poor, we have practically no Puerto Ricans, and we have a large rural population. Obviously, all of these things are going to enter into the fact that we have less illegal abortion here than we have in other states. I think the one per cent is somewhat like an iceberg, 99 per cent of which is below the surface.

Question:

Has an obstetrician or other practicing physician been sued for doing a therapeutic abortion in Minnesota after one of these committees has given its permission to go ahead?

Answer:

Only in the State of Pennsylvania has a physician been brought to trial for performing a therapeutic abortion. This man was found not guilty. There has never been one conviction in the United States where a physician has done a therapeutic abortion in a licensed hospital.

Question:

Now surely, gentlemen, this is a critical situation! If you will ask yourself when this occasion arises: Do we have sufficient justification for carrying out the destruction of a child? Do we destroy those babies who have damaged eyes and other defects when they are born? Do we destroy them in the last trimester of pregnancy because they do not have souls? Is there a difference between babies 24 weeks after conception and those after 25 weeks? Have they acquired souls in that one week?

Answer:

I do not have the answers to these difficult questions, and I am certainly no authority on religion. I find myself somewhat in agreement with St. Thomas Aquinas, who thought abortion was allowable before quickening. My point is that these underlying philosophical or theological assumptions are a road block to our finding out what the true situation is. Under the present state of our knowledge and under our present laws we cannot gather the necessary information and the conclusive evidence; this is the thrust of my argument.

*Ed Note: Extracted from the open discussion. Only the sting has been removed.

Continued

Question:

Will liberalization of the law decrease the number of criminal abortions?

Answer:

The very fact that we condone the breaking of a law does not mean we have to change the laws so that we do not break them. I do not mean to imply that liberalizing the abortion law in accordance with the recommendations made by the American Law Institute will decrease the number of criminal abortions. What I am saying is that there are women who are apt to seek criminal abortions if there are not enough physicians willing to do therapeutic abortions. You said that you and the Department of Psychiatry have a perfectly satisfactory arrangement. It may be perfectly satisfactory for the Department of Psychiatry, it may be perfectly satisfactory for the Department of Obstetrics and Gynecology; but I am not so sure that this is perfectly satisfactory for the individual patient.

I hope that you are familiar with the law, because if you are, you realize that any of you who have performed a therapeutic abortion are in a sense felons as the law stands in the Minnesota statutes at present, because it is an extremely rare situation where the life of the mother is preserved even by a medical indication for therapeutic abortion, and to me this is the crux of the problem.

Question:

Are we to permit ourselves to stand in legal jeopardy, or by modification; according to the American Law Institute, will we be able to practice medicine as we understand it in every ethical relationship according to the law of the States?

Answer:

You will find that groups in these same societies are exhorting us to do something about our perinatal mortality. At the present time we are being criticized if we are unable to save more than 97 out of every 100 infants born. I think this problem is so emotionally charged that we find ourselves cheering for one side or the other much as at an Irish soccer match, forgetting the fact that we are primarily physicians and surgeons. We have taken the Hippocratic oath and our responsibility is primarily from the medical aspect of this problem. We, as a part of society, have a great obligation to try to join with the social economic thinkers in making this world a better place in which to live, but I do not feel that as physicians we should assume all the responsibilities for the socioeconomic problems of the world.

We'll excuse our guests, and the business meeting will convene in three minutes.

Derivatively Speaking

Haustrum — from Latin *hauster* (a drawer)



Abstracts, Briefs and Commentaries

PAGET'S DISEASE OF THE MALE BREAST

James Paget first noted and described cases of areolar eczema followed by female breast cancer in 1874. Darier, 15 years later, established the concept of Paget's disease by the characteristic cells in the epidermis of the nipple. This condition in the male breast is extremely rare. In 1964, Hutchin and Houlihan collected 12 male cases in the world literature and added one of their own, which is reported in detail. Microscopic examination following surgical mastectomy revealed Paget's cells, large, with pale cytoplasm and prominent hyperchromic nuclei, along the malpighian layer of the eroded epidermis. The mass in the breast revealed an infiltrating distal carcinoma. Lymph nodes from the axilla contained metastases.

COMMENT: Paget's disease is said to comprise three to five per cent of all breast cancers, with cancer of the male breast estimated to be one per cent of the frequencies in women. Moss reported one case of Paget's disease out of 50 per cent of male breast cancers. Treves found two cases among 146 and Orase found one among 72 male breast cancers.

Hutchin and Houlihan classified Paget's disease of the male breast in three clinical types: (1) Paget's disease with nipple erosion only; (2) Paget's disease with nipple erosion and a palpable breast tumor; (3) Paget's disease with breast tumor alone. Nipple erosion with palpable breast tumor characterized most cases.

Surgery is the same as for similar carcinomas of the breast in women. The skin incision should be wide and, because of the absence of relaxed tissue as present in the female, skin grafting is usual. The cure rate of cancer in the male breast is comparatively low; Moss reported the five-year survival rate of 248 cases of male breast carcinoma to be 41 per cent. Poor results are due to: (1) hormonal environments quite different in each sex; (2) delayed medical attention in male patients; (3) the smaller size of the male breast, with early tumor infiltration of underlying tissues, skin, and regional lymph nodes.

Paget's disease with erosion of the nipple alone is frequently seen by physicians and dermatologists before a diagnosis is made.

Haagensen suggests that all erosions and dermatitis-like lesions which involve only the nipple epithelium are carcinomatous. Erosions that in-

Continued

volve the areola only or skin of the adjacent breast, leaving the nipple uninvolved, are not Paget's carcinoma.

Stanley R. Maxeiner, Sr.
Minneapolis, Minnesota

Suzuki, Takashi and Kubota, Nobutaka, Kyoto, Japan: Paget's Disease of the Male Breast, A Case Report. Surgery 92:6, 1966.

INSTRUMENT PERFORATION OF THE ESOPHAGUS — WHAT IS CONSERVATIVE MANAGEMENT?

The author describes the treatment of 16 patients who had had 17 instrument perforations of the esophagus during endoscopy. Nine patients had perforations high in the esophagus and ordinarily associated with no organic lesion. All underwent cervical drainage with or without closure of perforation within less than eight hours and received conventional doses of antibiotics. Average hospitalization was eight days. Eight patients had perforation associated with lesions of the thoracic esophagus (achalasia,* carcinoma, benign stricture). Six patients survived and the average hospital stay was 15 days. All had thoracotomies, and four of the surviving six had definitive treatment of their lesion.

The author discussed the "mental attitude" of the endoscopist when perforation had occurred. He felt that definitive surgical therapy was more "conservative" management than nonoperative approach for perforation. This avoided a second thoracotomy if a lesion was present; it also resulted in lower morbidity and mortality.

Comment: A thought-provoking and interesting article that should be carefully considered by all endoscopists.

Jerome Grismer, M.D.
Minneapolis, Minnesota

*See Test Your Word Score Page 63.

Groves, Laurence K.: Instrument Perforation of the Esophagus — What Is Conservative Management? J Thorac Cardio Surg 52:1, 1966.

CURRENT APPROACH TO THE SURGICAL MANAGEMENT OF EMPHYSEMA

The current approach to selection for operation is reviewed. Basically, the various tests search for patients with space-occupying, non-functioning lung encroaching upon adjacent more normal lung tissue. The type of surgical procedure preserves the most of normal pulmonary tissue. Nineteen patients had a total of nine bleb excisions, nine lobectomies, and two plications with "denervation." There were no operative deaths but four late deaths, three from respiratory failure within 24 months. Tracheotomy was used in nine patients.

Although there was immediate subjective improvement in 11, only five maintained this. Pulmonary function tests did not improve postoperatively.

The authors are seeking to correlate objective factors (angiography, lung scan, work of breathing, etc.) with subjective factors. In select patients the operations appear rewarding.

Comment: A difficult disease to treat by any method, emphysema offers a challenge to each and every physician. Because of its chronicity in the patient, the physician becomes dulled to aggressive management, continued reevaluation, and objective tests as to the result of therapy.

Jerome T. Grismer, M.D.
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Benfield, J. R., Cree, E. M., Pellett, J. R., Barbee, R., Mendenhall, J. T. Hickey, R. C.: Current Approach to the Surgical Management of Emphysema. Arch Surg 93:59, 1966.

BORIC ACID POISONING

An infant boy seemed in good health until, when he was three weeks old, his mother noted purplish mottling of his face. Next day he did not take the bottle well, was "breathing very hard" and vomited. He became less responsive and his respirations were irregular. He was dead when taken to St. Christopher's Hospital.

After the autopsy the child's mother related that she had dusted his diaper area freely with pure boric acid powder at every change of diapers for several days before his death. She had been told by her mother that boric acid was the best remedy for the infant's diaper rash.

Autopsy revealed much vacuolization of the acinar cells of the pancreas. Many of these vacuoles contained definite inclusions, some acidophilic and other faintly basophilic. Unfortunately the tissues were lost before toxicologic surveys could be performed but the mother produced an almost empty cardboard container of U.S.P. boric acid which she had been using, and there was no doubt of boric acid poisoning.

In two other fatal cases of boric acid poisoning in infants toxicologic examinations were performed. In both cases inclusion bodies were demonstrated in the acinar cells of the pancreas.

Intercytoplasmic inclusions in the pancreas due to boric acid poisoning were first reported by Fisher in four autopsies in 1951. He concluded that this finding alone was diagnostic of the disease. Greater awareness of the occurrence and significance of this apparently specific morphologic change would be valuable to pathologists in general and particularly to those dealing with infants and children.

Of 172 published cases of boric acid poisoning 83 were fatal; 78 were in adults and 94 in children. Boric acid poisoning still occurs frequently: at the Poison Control Center of New York City from 1955 to 1960 185 accidental cases were recorded. Of the 158 cases of household poisoning with boric acid reviewed by Gold in 1949, 30 were due to the application of pure boric acid to the denuded diaper area, and 23 were fatal.

Lister first used boric acid as an antiseptic in 1875, and it is still used extensively by the medical profession and others. Apparently many professional and nonprofessional people are not aware that this drug can be lethal. For every conceivable medical use of boric acid there now seems to be a more effective and safer agent.

In concentrations over 2 percent boric acid inhibits phagocytosis, and at 4 percent its toxicity to the tissues is greater than its bactericidal activity. When it is dispensed by drugstores to lay customers the containers should be clearly labeled "poison."

Courtesy of World-Wide Abstracts

Valdes-Dapena, M., and Arey, J. *J Pediat* 61/4:531.

Moliere on Doctors — II*

Seventeenth century French audiences were delighted with Moliere's Physician In Spite Of Himself (Le Medecin Malgre Lui), wherein the author satirized the medical profession of his time. In this gay and uninhibited comedy Sganarelle, a mere woodcutter, is prevailed upon to don the conventional physician's gown and peaked cap and impersonate a doctor to prescribe for a lovesick girl who is feigning muteness — with inability to utter more than a series of anks, eeks, and onks. In diagnosing the case Sganarelle pontificates:

"I maintain that this obstruction to the tongue's action is caused by certain humours, which we scientists call peccant** humors. Peccant, that is to say . . . peccant humors. Since the vapors caused by the exhalation of the influences which arise in the diseased area, arriving. . . you might say . . . at . . . Now these vapors I refer to, making a passage from the left side, where the liver is, to the right side, where the heart is, it comes about that the lungs, which we call in Latin *armyan*, having a communication with the brain, which we term in Greek *nas-mus*, by means of a vena cava, which we denominate in Hebrew *cubile*, encounter on their path the aforesaid vapors — because the aforesaid vapors have a certain malignity, which is caused by the acridity of the humors engendered in the concavity of the diaphragm, it then happens that the vapors — ossabundus, nequeys, nequer, potarinum, quipsa milus. And that is exactly how it comes about that your daughter is dumb."†

Vastly impressed, yet slightly puzzled by this unmitigated gobbledegook, Geronte, the girl's father, ventures:

"There is just one thing that bothers me: the position of the liver and the heart. It seems to me that you place them wrongly; and the heart is on the left side, and the liver on the right."†

This slight incongruity Sganarelle cavalierly dismisses by announcing:

"Yes, that is the way it used to be. But we have changed all that; now we use an entirely new method in medicine."†

Whereupon the subdued Geronte murmurs:

"Oh, I didn't know that. I ask your pardon for my ignorance."†

After a felicitous outcome for which the imposter Sganarelle deserves none but takes all the credit, he concludes:

"If things go on this way, maybe I'll stick to medicine for the rest of my life. I think it's the best trade there is, for whether you do well or badly, you get paid just the same. We never get blamed for doing a bad job; and we cut the cloth we work on to please ourselves. A cobbler making shoes can't spoil a piece of leather without paying for the damage; but in this job we can spoil a man without its costing us a penny. The blunders aren't our fault; they're always the fault of the man who dies. In short, the nice thing about this profession is that dead men have a marvelous decency and discretion; you never hear a dead man complain of the doctor who killed him."†

Whereunto an associate replies:

"It is true that the dead are uncommonly polite on this subject."†

*See Part I, Minnesota Med 49:1834, 1966.

**See Test Your Word Score Page 63.

†Moliere: Physician In Spite Of Himself: Translated from the French by Morris Bishop



Book Reviews

Books were only invented to aid the memory. — Petrarch

SYNOPSIS OF NEUROLOGY — Second Edition, Francis M. Forster, C. V. Mosby, Publication Date 7-15-66, Price \$7.50.

This small nicely bound synopsis is written by a single author and is quite readable. Its purpose is to instruct the reader in the manner of evaluating a patient from a neurological standpoint and to point up the highlights of the major neurological disease entities. It should prove to be valuable to students wishing to review the field but will be of little help to the clinician for refinements in diagnosis; and treatment of specific disease entities are necessarily deleted.

Harrison H. Farley, M.D.
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EPIDEMIOLOGICAL STUDY OF CANCER AND OTHER CHRONIC DISEASES — National Cancer Institute, Monograph 19, January 1966, U. S. Department of Health, Education and Welfare, Public Health Service, National Cancer Institute, Bethesda, Maryland, 465 pages.

This monograph is dedicated to the career of Harold Dorn, distinguished statistician, who died in May 1963. Dorn initiated the massive study of smoking done in recent years on government life insurance policy holders which continued from 1954 to the present. From this study a few impressive statistics can be quoted. An eight-and-a-half-year follow-up of just under 300,000 U. S. Government life insurance policy holders showed the following increased mortality risks associated with cigarette smoking, compared with those who have never smoked: 1.7 for deaths from all causes, 10.9 for lung cancer, 12.2 for emphysema, and 1.6 for coronary heart disease. Paralysis agitans is the only cause of death associated with significantly lower mortality for smokers than for nonsmokers. The risk for cigarette smokers was much greater than that for pipe or cigar smokers. Current smokers of cigarettes, pipes, or cigars experienced a mortality risk significantly greater than for nonsmokers, if they smoke more than four pipes or four cigars daily, or more than an occasional cigarette.

The very high degree of association found between cigarette smoking and death rates from pulmonary emphysema is paralleled by histologic findings of a close association between cigarette smoking and changes in the lung parenchyma,

including rupture of alveolar septa, fibrosis and an increase in thickness of walls of small arteries and arterioles. The association found between cigarette smoking and death rates from coronary heart disease is paralleled by histologic findings of a high association between cigarette smoking and the degree of atherosclerosis in the coronary arteries. The major portion of this monograph concerns studies on cigarette smoking and cancer.

This monograph is a reference work providing the statistical evidence of the pathological effects associated with smoking. It is not recommended for reading by the general public or by the general medical public. However, that portion of the medical profession which still persists in smoking, if they consider themselves still amenable to a logical argument, might benefit from perusal of the Dorn study of smoking and mortality among U. S. Veterans reported in this work. There is no logical ground left for the physician who denies the ill effects of smoking. The arguments for smoking are reduced therefore to illogical arguments. It is difficult to attack an illogical position with a barrage of logic. The smoker retreats into the realm of fantasy to protect his habit. This reviewer has been singularly unsuccessful in his attempts to control the smoking habits of his patients.

Reuben Berman, M.D.
Minneapolis, Minnesota

INTERNATIONAL SYMPOSIUM ON GENES AND CHROMOSOMES — Edited by: Professor Juan I. Valencia and Dr. Rhoda F. Grell. For sale by: The Superintendent of Documents, U. S. Government Printing Office, Washington, D. C. 20402. Price: \$3.50

This book is National Cancer Institute Monograph No. 18, published December, 1965, by the U. S. Department of Health, Education, and Welfare, Public Health Service, National Cancer Institute, Bethesda, Maryland, and is the proceedings of the International Symposium held at Buenos Aires, Argentina, November 30 to December 4, 1964. This book would be of limited value to a practitioner of medicine in the diagnosis or treatment of his patients. However, this symposium on research and teaching in bacterial genetics and human cytogenetics would be a valuable addition to the library both for study and for reference for any researcher in these fields.

Warren J. Warwick, M.D.
Minneapolis, Minnesota

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Special Article

The Abortion Problem

J. L. McKELVEY, M.D.*
Minneapolis, Minnesota

THERE ARE serious stirrings by small but vocal groups of mixed physicians, pastors and laymen who advocate the liberalization of the indications for abortion in the human. Such groups have organized themselves both in Los Angeles and in New York City. A similar start has been made in Minnesota. It is difficult to be certain just what these proponents wish. Some statements suggest a desire for liberal laws which accept present practice. But may this not really be an initial move toward a gross extension of the legal indications for induction of abortion. Most of the proponents are frank about this.

Groups of physicians have been questioned as to their attitudes. It is difficult to know how representative these groups are or how much they have read or thought about the problem. They are quoted as being largely in favor of extending the indications for fetal destruction.

Those who have serious doubts as to the wisdom of such change and as to the reliability of the data on which it is proposed have either hesitated to argue publicly or given the impression that they speak from rigid prejudice. It would seem that this whole matter is important enough to justify an attempt to examine it with as much objectivity as any of us can muster. The hope is that this will lead to some careful thinking.

There are two chief arguments for changing the present legal status of therapeutic abortion. *The first is* that, in general, the law is so out of date that the responsible physician is forced into occasional illegal acts in order to adequately care for his pa-

tients. The threat of punitive legal action has stopped some physicians from doing what they consider right and has led some hospitals to forbid such procedures. *The second argument* is that this attitude has forced patients, particularly those who are poor, into the hands of criminal abortionists with the attendant risks of permanent damage or destruction. It is assumed that if abortions could be obtained at the wish of the patient, they would be done in hospitals and these risks would disappear.

The proponents generally support a 1959 recommendation of the American Law Institute. Their model for legislative action by the states was as follows: "A licensed physician is justified in terminating a pregnancy if he believes there is substantial risk that continuance of the pregnancy would gravely impair the physical or mental health of the mother, or that the child would be born with grave physical or mental defects, or that the pregnancy resulted from rape or incest."

One may be justified in some concern when this is followed by: "But for millions of other women with valid reasons for desiring an abortion, there can be no safe, painless, legal solution to their plight." "The medical profession is intimidated and confused. In the name of observing the law, shameful injustice is committed."** "They fail to recognize—the serious danger to persons or families faced with unwanted pregnancies."† The indications would thus be extended to "desiring an abortion" and an "unwanted pregnancy."

It is clear that the acceptance of all of this involves of necessity an agreement with the conclusion that the child or fetus or whatever one wishes to call it is not a devel-

Continued

*Head, Department of Obstetrics and Gynecology University of Minnesota Medical School.

**Lawrence Lader, *New York Times* magazine section.

†Dr. Kenneth R. Niswander, Medical School of the State of New York at Buffalo.

oping human or that it is without any claim to the right of protection and so may be destroyed without compunction at the convenience of an adult. Is this acceptable by the thoughtful physician?

The Law

There are said to be no Federal laws dealing with abortion induction. The states have handled the problem in a variety of ways.

Preservation of Life and Health

The details of these do not need to concern us here. In general, they allow the interruption of a previable pregnancy for the purpose of "the preservation of life and/or health of the mother." An occasional strange one adds the life and health of the fetus. The value of an abortion for this purpose is not clear. In some states the only indication is the preservation of the life of the mother. There is, I believe, no state which has legalized as an indication a possibly damaged fetus. The dreadful thalidomide experience and the more recent confusing publicity about intrauterine rubella infection has brought this back to the fore. It is clear then that doctors have been acting in disregard of the law in two directions. They have been doing abortions which had no legal justification. And they have been dishonestly ascribing the indication for abortion to the preservation of the mother's life or health when they knew very well that this was untrue.

Rubella

Some reputable physicians in San Francisco have aborted women who had rubella in the first trimester. They purposefully brought this to the attention of the local law enforcement authorities who were thus forced to act. Most of us are seriously disturbed about this. It would seem that a lay jury inflamed by emotional lawyers is scarcely the ideal quiet reasoning group to decide such an issue.

There are a considerable number of problems which stand in the way of an ideal solution. Let us ask ourselves a few questions.

Purpose of the Law

What is the purpose of an abortion law? It is clearly the expression of a sort of public

consensus that it is wrong to destroy a developing human. The developing human fetus or baby or whatever one wants to call it can produce serious embarrassment to adults under a variety of circumstances. There is, then, the temptation to destroy it. The accumulated wisdom of a sort of common law concludes that this is wrong and has set up penalties for unjustifiably yielding to the temptation.

Preservation of Host

Gradually, certain qualifying situations have developed. The physiologic and, in some cases, pathologic changes in the host which are the result of pregnancy can on occasion produce destructive effects on specific organ systems so that the host's life is endangered. Under these circumstances the fetus and placenta are aggressors. The practical feature is of course that if the mother dies the previable or aborted fetus will also die. Does one allow both to die or is there justification for removing the pregnancy in the hope of preserving the mother's life? Medical opinion would seem to agree on this. The catch lies, of course, in the skill, the judgment and the honesty of the physician who determines the risk. How great should the risk be to justify interference? These are things which can be neither adequately described in a law nor reasonably decided in a court room. How much risk of progression of a maternal disease process justifies destruction of a child? How accurate is the assessment of this degree of risk?

Moral Law

The public has realized this and has placed an astonishing degree of faith in the careful honesty of the physician. They have tolerated his breaking of the law on occasion with the assurance that he will act with good medical judgment and complete honesty. No physician need fear the law under these circumstances. It is not right to say that the medical profession is intimidated and confused. I am not. But it should be perfectly clear to all physicians who are involved in these things that the very fact that such laws are broadly written and that the public trusts the physician to do his

own interpreting, puts on the medical group the responsibility to think clearly, to act with complete intellectual honesty and to discipline itself to stay within the limits of generally accepted morality. The physician must not run off on his own radical path when it involves the public trust and the taking of a life. All of us know and can document the fact that this is not universally accepted, which is a pity.

The public has gradually softened its attitude toward the mother who aborts herself or obtains what is known as a criminal abortion. There was a time when the law under the influence of the Christian Church actually required the crucifixion of such women. This sympathy seems to have spilled over on the criminal abortionist, who is likely to be given only a minor penalty unless the mother has been killed as well. Now there appears to be an organized push to greatly extend the indications for abortion.

British Common Law

This involves some strange thinking. The world was horrified when Hitler destroyed children en masse. All of us would bitterly condemn one who wilfully destroyed a recently delivered viable baby. This includes, of course, the premature delivered after 28 weeks of pregnancy. British common law separated infanticide as a crime and abortion as a misdemeanor at the time the fetal movements are felt, which is usually about eighteen weeks after the last menses. It would seem that a widely held opinion has developed which holds that suddenly at about this four to five-month point something happens which changes a piece of living tissue like an appendix into a human with rights of protection. What is this change and when does it occur? People who pretend to some specially dispensed information not available to the general public have given what they consider to be learned dissertations on the soul and its entry into the developing human. What is this soul? Where is it? When does it enter a developing fetus? At one time it was concluded by the learned that the soul entered the body of the male and the female at different durations of pregnancy. What evi-

dence is there to support all this? What evidence is there that a baby at three months of development is different in this respect from one at four or five or six or ten lunar months? You can amuse yourself with the silly arguments in the literature dealing with these points. The Yen-an Chinese will not bury a young child in the same burial place as the adult because, in their considered opinion, the child's soul had not yet entered him. Does the intelligent person dare to use this sort of reasoning to decide when his responsibility to another human begins? And, if he cannot do this as an individual, how can the group apply this to the extension of a rational law? It should be clear then that destruction of an intra-uterine fetus at any point in its career is infanticide and can be justified only under the most exceptional circumstances. In the University of Minnesota clinical material, this appears to occur once in about four or five years. The indications do not include "millions of other women with valid reasons for desiring an abortion," or "the persons or families faced with unwanted pregnancies." There are solutions for these difficulties short of taking a human life, and personal experience has borne out the effectiveness and reality of this conclusion.

American Law Institute

In the light of all of this, let us look at the details of the model code recommended by the American Law Institute. What is meant by the adjective substantial? Can this be interpreted so that a commonly accepted definition could be achieved? This would allow — as you very well know — the finding of an excuse to abort every woman who requested it. Every unmarried mother, every patient with anemia, with three other children, with a drunken husband, or who can claim to be depressed will be prime candidates. These indications are not reasons for fetal destruction, but they have been and will be used as excuses to get rid of a pregnancy which the patient doesn't want at the moment. If this involved only hospitalization, some anesthesia and a minor surgical procedure, one would shrug his shoulders and

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not worry too much. Unfortunately, it involves taking a life and that is another matter.

Very strange things are presently going on which involve the interpretation of indications for abortion. The interested reader is referred to a study by Dr. Robert Hall (*Am. J. Obs-Gyn.* Vol. 91:No. 4: p. 518, February 15, 1965) which details the experiences of Columbia University Medical School at Sloane Hospital in New York City. The experiences of a great many other hospitals throughout the country are listed. One hospital in New York City listed 4501 ward deliveries (1960-1962) and five abortions (1:900) as against 2023 private patient deliveries with 101 abortions (1:20). How do you interpret this? What are the realities of the indications which are being applied? What is meant by "substantial risk?" Do we really wish to legalize abortion for each twenty term pregnancies? To kill one baby in twenty?

Indications

The indications for destruction of pregnancies seem to change rapidly. In one hospital, the ratio of abortions to live births was 1:141 for ward and 1:37 for private patients. A therapeutic abortion board was established whose permission was required for the procedure. Following this the ratio was 1:429 for ward and 1:111 for private patients. The obvious questions do not need to be listed. What would be the effect of the application of a rule of "substantial risk?"

Some time ago, the indications were largely based on organic disease. Gradually these were demonstrated to be for the most part either unreal or problems which could be handled by other means than abortion. It is fairly easy to document the proof of this so that disagreement is hard to justify. An astonishing shift has now occurred, largely in the private patient group. The indications are now psychiatric in about two thirds of the patients. These are much harder to document. Most of us have come to the conclusion that there is no psychiatric indication whatever for abortion. The psychiatric problems can be handled effectively in other ways. The suicide rate in women is less than

in men by 4 or 5 to 1. Depressions can be recognized and treated. There has been no suicide in an unmarried mother in Minnesota since 1957. There is no psychiatric disease which can be cured by abortion. There are some very obvious questions to ask about the sudden shift of indications and the strange difference between the indications in private and in ward patients. Again it isn't necessary to list these.

Intrauterine Damage

The problems associated with the possibility of intrauterine damage from chemicals or infections have suddenly come to the fore. The infection about which most is known in detail is that of syphilis. Oddly enough, this did not raise the question of mechanically destroying the fetus of an infected mother. Attention was focused on rapid recognition and treatment of the disease, which eventually proved to be remarkably effective. Let us remember that forty or fifty years ago, syphilis in the pregnant mother was infinitely more frequently encountered than rubella in recent times and that the fetal infection rate and the resultant disasters were at least as severe. It was, then, a much greater problem than rubella. Should we have destroyed somewhere between 5 and 15% of the fetuses because of the risk of fetal syphilis?

This leads on to the worrisome features of the model code inclusion of "substantial risk—that the child would be born with grave physical or mental defects." What is the order of "substantial risk" here? Since rubella infection is the major application of this at present, let us look at a sample of what we know of this risk. This is done with the clear understanding that there seems to be good evidence that the risk to the fetus varies in different epidemics.

Rubella In First Trimester
(Combined Reports of Lundstrom, Manson and Pitt)
Risk of Severe, Disabling Lesions In Surviving Child

Cataracts and blindness	2%
Severe deafness	6%
Disabling heart lesions	1%
Mental deficiency	1-1 1/2%
(Mental deficiency in general population)	1%
Real risk of one or more lesions	7-10%

This is the sort of information one must use in deciding what the order of a given risk may be. But this begs the question of the basis on which one will use it. Do I have the right to kill a considerable number of developing humans who are normal in order to get rid of the painful problems of the occasional child who is born alive with an abnormality which may be minor or severe? Understand that no one is cured of anything in the process. Do I indeed have the right to kill a human, developing or developed, because it has an abnormality? Is the three or four-month fetus a developing human? Each of us must answer these questions carefully and honestly for himself. It is perhaps absurd to suggest a compromise. If one believes that he is justified in destroying a child because it has an abnormality would it not be better to give legal blessing to waiting until the babies are born at term, letting those who are normal survive and handling the abnormal ones with a hammer since they are now too big for a curet? This is a horrible thought, but isn't it really more sensible and humane than indiscriminate destruction of the normals and abnormals, the so-called King Pharaoh technique? If I were a normal fetus at risk I should certainly think so. It is recognized that perfectly honest students of the problem will disagree. For myself, I cannot avoid the conclusion that my duty is to preserve life insofar as possible and that I have specifically sworn not to purposefully destroy human life. Like the syphilis problem, it would rather seem that we should try to control the disease. There is every reason to believe that this can be done. If one can convince the physician of the justification of these conclusions, the presence or absence of specific legal permission would seem to be of little importance. There is no desire to either punish the person who honestly disagrees or open the legal abortion door wide to the careless or dishonest person. The object is to encourage critical, responsible thought. The courtroom is not the place to achieve this.

What about the horrible problem of the baby who has been exposed to thalidomide

or methotrexate? Here the abnormalities are very much more frequent and more severe. One can only settle these problems for himself. The prime necessity is, of course, prevention. The reputable physician who depends on his own honest conclusions in this and a number of other infrequently occurring problems has no need of specific legal permission.

Rape or Incest

And what of pregnancies which result from rape or incest? It is difficult to define rape. There is good reason to believe that a vaguely large proportion of rape involves at least some cooperation and indeed is often an afterthought. If one puts a reward on such afterthought, as the legal removal of an unwanted pregnancy, the result may not be unexpected. The abortion door will be opened wide and the general public invited in. If the rape or the incest is real, destroying the fetus will not change the fact that it has occurred. It will only partially hide the evidence from the general public at the expense of destruction of the most innocent individual of the three. Again, is the three or four-month fetus a developing human? Can we take human life for the convenience of an adult? The simple fact is, of course, that there are other methods of sympathetic handling of the mother which are at least as effective as abortion. In spite of the fact that a British jury has disagreed, there seems to be no reason other than sympathy for specifically legalizing abortion for rape or incest. All of us will be sympathetic toward the girl and bitter toward the male who caused the disaster. We would do anything in the world to help her short of destroying an innocent individual.

What now are the advantages of changing the law? Under present circumstances, a reputable physician can carry out his decisions without fear of reprisal providing only that they satisfy the public consensus of what is reasonably justifiable. His colleagues or the hospital authorities will act as reasonable brakes but will support him in an honest informed decision.

Changing the law would appear, then, to

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have another significance. It is reasonable to assume that such change is designed to allow extension of the indications. For the reasons stated above, one must object to that.

Criminal Abortions

The Danger

There can be no question but that a great many women seek out dangerous methods of one sort or another to remove unwanted pregnancies. The degree of danger is likely to be related to the ability of the patient to pay the abortionist. Under ideal circumstances, abortions can be done with very little vital risk. The procedures which are open to the poor on the contrary can be very risky not only to the life of the individual but to her future health. If these abortions were indicated on the basis of the public consensus of what is justified, they could and many would be done in a qualified hospital, by a trained and reputable physician and so safely. The only conclusion is that they do not satisfy these requirements and so, since they involve destruction of a fetus, justify the term criminal abortion. No one knows how many of these are done or how many women are damaged or destroyed by them. Estimates which have been as high as 5 to 10,000 deaths from this cause each year in the United States would represent more than 150 as Minnesota's share. The detailed Minnesota Maternal Mortality Study is extremely unlikely to miss any of these. In actual fact, Dr. Alex Barno* has shown that there were 20 such deaths in Minnesota in 15 years to 1964 or $1\frac{1}{3}$ as a yearly average. Higher risk calculations are based on California and New York. It would seem clear that if one wanted to stop abortion deaths, the best solution would be to remove women of childbearing age from these states. The incidence per unit of population elsewhere may be greater than in Minnesota but not that much greater. The suggestion is that the estimate is excessive.

Suffering and Damage

The suffering and damage, both physical and emotional, is unquestionably great and

one would like to do anything he could to remove even a part of it. It has been suggested that if the indications for legal abortion were extended to include the simple wish to get rid of an unwanted or embarrassing pregnancy, this suffering could be avoided, and "millions of other women with valid reasons for desiring an abortion —" (Lader) would be happily and safely treated in reputable hospitals. There is evidence from areas where abortions are carried out at the patient's wish that this hope has not been realized. What is perhaps more potent in considering this proposition is the same old issue. Are these developing humans and can we justify slaughtering them by the millions? Can one justify Pharoah's approach? What these people need is help, human comfort, and an arm around the shoulder rather than fetal destruction. I have been through this sort of thing so often that I feel justified in the conclusion that I am right and that the problems can be handled by other means. Indeed, they can be handled much better by other means.

William Ober, a pathologist in New York, lists the details of two patients in a series of very radical recommendations in the October 8, 1966 *Saturday Evening Post*. One is a 34-year-old married woman who had some sort of pelvic infection associated with an intrauterine fetal death at five months some seven years prior to the present problem. She is now pregnant again, which means that her pelvic infection is either cured or was originally questionable. "She became deeply fearful of having another pregnancy — and is terrified. For two weeks she has cried; she cannot stand the sight of her children." Dr. Ober wants her aborted. It does not require a special skill for the clinician to recognize a seriously emotionally-ill, depressed patient. She needs competent psychiatric care in a hurry. She will not be cured by an abortion and may even be made worse by this procedure.

Unwanted Pregnancy

The other patient is a fourteen-year-old pregnant by a friend of her father. He is described as "a perfectly reputable business man," which one finds hard to believe.

*See page 11.

Does one kill an innocent fetus because of this man's disgusting activities? Will this procedure wipe out the rape? Dr. Ober says, "I believe that every woman should be able to have an unwanted pregnancy aborted at her own request subject only to the consent of her husband and the advice of her physician." It is this sort of attitude which seriously worries the vast majority of thoughtful laymen and, I believe, of physicians. It is this sort of admission which justifies one's suspicion that it is not really a change in the law to conform to present day knowledge, but a vast extension of indications for abortion which these groups really intend. The alternative to this is the extension of social services, of related education, of available contraception and, where indicated, of sterilization. Above all, doctors and nurses must be ready to offer kindness, understanding and patience to the distraught woman. She needs a friend and help rather than an abortion or a changed law. The problem really is to find her and to get her into such hands.

Indications for Abortion

It is not possible to go extensively into this field. A good deal of the problem has already been mentioned. Prevention of the difficulties is, of course, an ideal solution and the application of this is obvious. There are some medical or surgical indications for therapeutic abortion which are still accepted, but the vast majority of these have vanished in the light of experience and factual data. In general, the removal of a pregnancy is justified only when it can be demonstrated to be a really dangerous aggressor.

Some very strange things have been turned up in studies of indications which have been applied. The astonishing dissimilarity of the incidence of indications in those who can and those who cannot pay for the procedure has already been mentioned. It could be held that the private patient rate is justified and that the underprivileged group are having adequate medical care in hospitals withheld from them in spite of the fact that, in many instances, both groups are being cared for by the same staffs. Logically this should move the abortion incidence in

the opposite direction for a number of reasons.

In another study, 40% of those aborted were unmarried, widowed or divorced. The indication here would seem to be readily identified as the convenience of an adult.

In still another study, done in Sweden in 1958, 100 women who had been aborted in the interests of "the health of the mother" were followed. Within three years, 70% of them were pregnant again and delivered without a single serious complication. In still another, 50 were given permission for an abortion but decided against it. There were no deaths in the group and "nine reported improvement in their mental health." The confusions here are obvious. The original indications were largely non-existent.

Psychiatric

The most confounding aspect of the problem is the psychiatric one. There can be no doubt of the reality of the sudden switch from the indication of organic disease to that of emotional disturbance. In one study, psychiatric indications changed from 15% in 1940 to 80% of the hospital abortions at present. One is constantly astonished at the apparently universal ease with which psychiatric consultation can be obtained to agree to abortion. The author knows of it being accomplished over the telephone without even seeing the patient. Apparently a large segment of the psychiatric group hold to the concept that "if a woman does not like being pregnant, she has a right to have it removed." No psychiatrist will ever tell me at what point in the duration of the pregnancy this changes, although all agree that it is best to destroy the child before it is born alive at term. Are these people right and are those of us who would deal more conservatively with our responsibilities to human life wrong and old-fashioned?

Let us be clear, however, about the reality of the arguments regarding a psychiatric indication. There is no psychiatric disorder which can be cured by an abortion. The author, in spite of repeated efforts, has never been able to get a psychiatrist con-

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sultant to write as part of the indication that the abortion will cure the psychiatric disorder. Indeed, the pregnancy may on occasion be used as a lever to pressure the patient into adequate psychiatric care. As in some organic diseases, so here. The patient may well be better off pregnant and adequately treated than not pregnant and without treatment.

Risk of Suicide

In the socially troubled and depressed patient, the risk of suicide has been given as an indication. Lindberg has followed 27 women who were pregnant and threatened suicide. No single one carried out the threat. Barno has studied the Minnesota material. There were 14 suicides in pregnant woman in the 15-year study and among 75 to 80,000 live births a year or among a total of 1,232,500 live births. This is about 1 per 100,000 live births per year as compared to 3.1 to 5.2 per 100,000 females of all ages. There was no single suicide in an unmarried mother. There were two schizophrenics and 12 psychotic depressions. At least these 12 should and, in most instances, could have been recognized and appropriately handled. Ten of the 14 committed suicide post partum, so that a physician had an excellent chance to recognize the risk. He had had them under his care during the stress of pregnancy and delivery. Indeed four of the 14 were under psychiatric care. In none of the 14 had there been a request for abortion. It would appear then that the pregnant woman in Minnesota carries $\frac{1}{3}$ to $\frac{1}{5}$ the suicide risk of the general female population and that those who do commit suicide can largely be prevented from doing so. This can then scarcely be considered as a real indication.

Passage of Heredity

One is more concerned about the hereditary or environmental passage of the emotional disturbance to the child. The second of these is probably much the more important of the two and its handling is obvious.

Sterilization of the chronically psychiatrically disturbed patient may be clearly indicated.

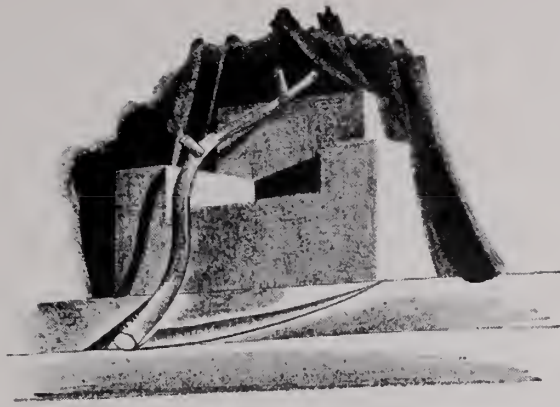
At the University of Minnesota, then, abortions are not done for psychiatric indications. The recognition and treatment of the emotional disorder is carried out instead; and, for what it may be worth, experience has shown this to be a satisfactory decision. The patient is sick, and the pregnancy is normal. Abortion for this reason then would not seem to be indicated. Should we encourage the reverse attitude by legalizing abortion for "the substantial risk of impairing the mental health of the mother" and, if so, who is to determine this and on what reliable data?

There are more data from studies dealing with the effect of the abortion on the emotional well-being of the patient. There is not time to consider this in detail. The author has been horrified to see the ravages of the guilt sense in a considerable number of women and their consorts who had undertaken criminal abortions. The end results of removing an unwanted pregnancy are certainly not as simple and uninvolved as one might think at first glance.

Conclusions

From all of this, there arises the hope that physicians and nurses and particularly our own group in this mid-Northwest will conclude that our voluntarily accepted duty is to try to progressively increase the efficiency with which we can save lives and obviate human suffering. And, unless we can establish without question the fact of a vital fetal aggression which cannot be handled in any other way, that we shall avoid the purposeful taking of a human life for whatever other reason and no matter what the law allows. For my own part, I shall struggle against a legal breach in the dike, however small, in the fear that a flood will follow. There is reason to believe that a flood is planned.

Success is a journey and not a destination. — Advertising Age



In Memoriam

We understand death for the first time when He puts his hand upon one whom we love. — DeStael

WALLACE E. ANDERSON, M.D.

Dr. Wallace E. Anderson, 58, Clearbrook physician, died November 12. Born at Wing, North Dakota, Dr. Anderson received his degree in medicine at the University of Minnesota. He was formerly associated with Dr. O. F. Melby at Thief River Falls; however, following his discharge from the armed services in 1946, he moved to Clearbrook where he has been practicing for the past twenty years.

Dr. Anderson was a past-president of the Red River Valley Medical Society, a member of the American Medical Association and the Minnesota State Medical Association.

He is survived by his wife and a son.

EARL BRUCE TRUCKER, M.D.

Dr. Earl Bruce Trucker, 34, pathologist at the Hennepin County General Hospital, died November 28. Born in Minneapolis, Dr. Trucker graduated from the Harvard Medical School in 1958.

He was a member of the Hennepin County Medical Society, Minnesota State Medical Association, and the American Medical Association.

He is survived by his wife, three sons, and a daughter.

HENRY B. CLARK, JR., M.D.

Dr. Henry B. Clark, Jr., professor and head of the department of oral surgery in the University of Minnesota's School of Dentistry, died December 3, after a long illness. He was born in Oak Park, Illinois, and graduated from the University of Minnesota with a doctor of medicine degree in 1933. He interned and then entered the School of Dentistry in 1936.

Dr. Clark served on the board of directors of the

Minnesota Cancer Society, was president and counselor of the Minnesota section of the International Association for Dental Research; served on the international professional relations committee of the Ramsey County Medical Society; was president of the Minnesota Society of Oral Surgeons, a member of the Ramsey County Medical Society, Minnesota State Medical Association and American Medical Association.

He is survived by his son and three daughters.

ROGER W. MARKS, M.D.

Dr. Roger W. Marks, 54, former Dakota County coroner, died December 25, in St. Luke's Hospital, St. Paul. He had served as coroner eight years and resigned last September because of illness. Born in St. Paul, he graduated from the University of Minnesota Medical School.

He was a member of the Ramsey County Medical Society and American Medical Association and an associate member of the Minnesota State Medical Association.

He is survived by his wife and two daughters.

HENRY JOSEPH REIF, M.D.

Dr. Henry J. Reif, 58, St. Cloud physician, died December 21. He was born in St. Paul and lived there for thirty years before moving to St. Cloud in 1946 where he had a general practice. He was a graduate of the University of Minnesota Medical School.

He was a member of the Stearns-Benton County Medical Society, Minnesota State Medical Association and the American Medical Association.

He is survived by his wife, two daughters and two sons. Dr. Robert W. Reif of White Bear Lake is his brother.

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facilities of medical schools and teaching hospitals. Such cooperation leads toward more effective care of more patients—the common goal of medical and pharmaceutical research—toward reduction in the cost of disease, toward increase in useful longevity.

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Mortality Study

Therapeutic Abortion*

Incidence and Indications in Minnesota

PHILIP N. BRAY, M.D.
Duluth, Minnesota

Therapeutic Abortion in the Four Largest Cities in Minnesota 1955-1964

ABBOTT HOSPITAL — MINNEAPOLIS

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	1,060	1,083	1,197	1,203	1,133	1,222	1,130	1,050	877	945
Therapeutic abortions	1	2	2	2	0	4	1	0	0	0
Total live births: 10,900 Therapeutic abortions: 11 Ratio: 1:991										

Year	Indications	Committee Rules
1955	Rheumatic heart disease.	All therapeutic abortions are approved by a Sterilization Committee. Three (3) members of this committee shall constitute a quorum.
1956	Renal hypertensive cardiovascular disease.	
1956	Bronchiectasis. Mitral stenosis from old rheumatic heart disease.	
1957	Quadriplegia from poliomyelitis. Severe respiratory crippling from poliomyelitis.	
1957	Rheumatic valvular heart disease with mitral stenosis and aortic insufficiency.	
1958	Rheumatic heart disease.	
1958	Severe schizophrenia with suicide attempts.	
1960	Rheumatic heart disease with mitral insufficiency, mitral stenosis. Cardiac enlargement.	
1960	Multiple sclerosis.	
1960	Myoma of uterus. History of carcinoma of breast with metastasis.	
1960	Acute depression. Hereditary retardation.	

ANKER HOSPITAL — ST. PAUL

Births	1955 through 1964	Total:	7,698
Therapeutic abortions	1955 through 1964	Total:	3
Ratio: 1:2566			

Year	Indications	Committee Rules
1962	Kidney disease.	No information given on the Therapeutic Abortions Board.
1964	Psychiatric.	
1964	Psychiatric.	

*Part of the Symposium on Therapeutic Abortion read at the meeting of the Minnesota Obstetrical and Gynecological Society, Rochester, April 23, 1966.

Continued

MORTALITY STUDY

ASBURY — METHODIST HOSPITAL — MINNEAPOLIS

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	631	777	748	646	1,513	1,661	1,744	1,739	1,758	1,811
Therapeutic abortions	0	0	0	0	1	0	0	0	0	2
Total live births: 13,028 Therapeutic abortions: 3 Ratio: 1:4343										

Year	Indications	Committee Rules
1959	Psychiatric indication — Depressed, suicidal and homicidal tendencies.	The Sterilization and Therapeutic Abortion Committee is composed of 2 Obstetricians, 1 Internist, 1 Psychiatrist and 1 Urologist. A majority vote rules.
1964	Chronic glomerulonephritis with persistent albuminuria. Hypertension.	
1964	Chronic pyelonephritis with hypertension and uremia.	

BETHESDA LUTHERAN HOSPITAL — ST. PAUL

Births	1955 through 1964	Total:	18,358
Therapeutic abortions	1955 through 1964	Total:	7
Ratio: 1:2623			

Year	Indications	Committee Rules
1955 through 1964	No information given on indication.	The Therapeutic Abortions Committee is composed of 2 consulting physicians — one a specialist in the field and one a hospital staff member.

EITEL HOSPITAL — MINNEAPOLIS

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	586	681	547	671	565	497	458	645	652	673
Therapeutic abortions	0	0	1	0	0	0	0	0	0	0
Total live births: 5,970 Therapeutic abortions: 1 Ratio: 1:5970										

Year	Indications	Committee Rules
1957	Otosclerosis with likelihood of severe progressive hearing loss.	The Sterilization Committee is composed of 2 obstetricians, 1 urologist, 1 psychiatrist and 1 internist.

FAIRVIEW HOSPITAL — MINNEAPOLIS

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	Individual years not given									
Therapeutic abortions	Individual years not given									
Total live births: 24,982		Therapeutic abortions: 3			Ratio: 1:8,327					

Year	Indications	Committee Rules
1955 through 1964	Schizophrenic reaction. Chronic paranoid schizophrenia. Subacute glomerulonephritis. Hydatiform mole.	Administration and the Attending Physicians decide on Therapeutic Abortions.

THERAPEUTIC ABORTION — BRAY

GLENWOOD HILLS HOSPITALS — MINNEAPOLIS

Births	August 1958 through December 1964	Total: 7,735
Therapeutic abortions	August 1958 through December 1964	Total: 0
Committee Rules	The Committee is headed by an Obstetrician-Gynecologist with one member in Psychiatry, one in Surgery, one in Internal Medicine and one in General Practice. They are in the process of organizing a Sterilization-Abortion Committee.	

HENNEPIN COUNTY GENERAL HOSPITAL — MINNEAPOLIS

Births	1955 through 1964	Total: 10,775
Therapeutic abortions	1955 through 1964	Total: 0
Committee Rules	There is no Therapeutic Abortion Board.	

LUTHERAN DEACONESS HOSPITAL — MINNEAPOLIS

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births				Individual years not given						
Therapeutic abortions				Individual years not given						
Total live births: 11,619		Therapeutic abortions: 4			Ratio: 1:2902					
Year	Indications						Committee Rules			
1955 through 1964	Cancer, breast. Multiple sclerosis. Hypertensive A.S.V.H.D. Polio victim.						The Sterilization and Therapeutic Abortion Committee approves or disapproves by a majority vote on Therapeutic Abortions.			

MAYO CLINIC — ROCHESTER

Births	1955 through 1964	Total: 15,971
Therapeutic abortions	1955 through 1964	Total: 36
Ratio: 1:444		
Year	Indications	Committee Rules
1955 through 1964	1 case — carcinoma cervix. 5 cases — carcinoma breast. 4 cases — brain tumor. 1 case — chondrosarcoma (hind quarter amputation). 1 case — toxemia. 1 case — acute nephritis. 2 cases — chronic glomerulonephritis. 1 case — chronic pyelonephritis. 1 case — infected hydronephrosis. 1 case — chronic renal insufficiency. 1 case — pulmonary hypertension. 1 case — periarteritis nodosa. 2 cases — chronic ulcerative colitis. 2 cases — erythroblastosis (3 stillbirths apiece). 1 case — rubella. 1 case — schizophrenia. 1 case — socioeconomic. 1 case — Reynaud's disease. 1 case — multiple sclerosis. 1 case — myasthenia gravis. 1 case — Henoch-Schonlein purpura. 1 case — bilateral retinal detachment. 1 case — right hip osteomyelitis. 3 cases — diabetes.	The committee is composed of 2 in the Obstetrical-Gynecological Department or if in some other field, a consultant in that field.

Continued

MORTALITY STUDY

MIDWAY HOSPITAL — ST. PAUL

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	1,700	1,642	1,449	1,511	1,563	1,582	1,438	1,402	1,395	1,200
Therapeutic abortions	0	0	0	0	0	0	0	0	0	0
Committee Rules	The Sterilization and therapeutic abortion rules are being revised. No information given at this time.									

Total birth: 14,882

THE CHARLES T. MILLER HOSPITAL — ST. PAUL

Births	1955 through 1964	Total:	17,950
Therapeutic abortions	1955 through 1964	Total:	15

Ratio: 1:1197

Year	Indications	Committee Rules
1955 through 1964	No information given on indication.	Consultation of another physician (except in emergency) for Therapeutic Abortions.

MOUNDS PARK HOSPITAL — ST. PAUL

Births	1955 through 1964	Total:	4,065
Therapeutic abortions	1955 through 1964	Total:	0
Committee Rules	There is no Therapeutic Abortion Board.		

MOUNT SINAI HOSPITAL — MINNEAPOLIS

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	1,044	1,541	1,555	1,463	1,013	992	966	815	707	709
Therapeutic abortions	0	3	0	0	0	0	0	2	0	2

Total live births: 10,805 Therapeutic abortions: 7 Ratio: 1:1544

Year	Indications	Committee Rules
1956	Cerebral palsy.	The Sterilization and Abortion Committee is composed of 5 on the Staff — Chief of the Department of Obstetrics and Gynecology, a Psychiatrist, an Internist, Urologist and General Practitioner. A majority vote rules.
1956	Diabetic neuropathy.	
1956	Malignant hypertension.	
1962	Multiple sclerosis.	
1962	Psychosis.	
1964	Severe renal hypertension — Hypoplastic aorta.	
1964	Psychiatric — under psychiatric care.	

NORTH MEMORIAL HOSPITAL — MINNEAPOLIS

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	423	1,018	1,324	1,327	1,406	1,492	1,723	1,681	1,671	1,917
Therapeutic abortions	0	0	0	0	0	0	0	0	0	0
Committee Rules	The Committee consists of a chairman in Internal Medicine and 4 members — Obstetrics-Gynecology, Psychiatry, Neurology, General Practice and Urology. Two-thirds (2/3) majority vote rules.									

Total births: 13,982

THERAPEUTIC ABORTION — BRAY

NORTHWESTERN HOSPITAL — MINNEAPOLIS

	1955-59	1960	1961	1962	1963	1964
Births	Not available	1,706	1,705	1,681	1,592	1,399
Therapeutic abortions		1	2	1	0	3

Total live births: 8,083 Therapeutic abortions: 7 Ratio: 1:1169

Year	Indications	Committee Rules
1960	Carcinoma of breast with prior radical mastectomy.	The Sterilization and Abortions Committee is composed of 5 members — 2 Obstetrician-Gynecologists, 1 Urologist, 1 Psychiatrist and 1 Internist. A majority vote rules.
1961	Emotional health.	
1961	Psychiatric.	
1962	Psychiatric.	
1964	Rubella in early pregnancy.	
1964	Psychiatric.	
1964	Rubella in early pregnancy.	

OLMSTED COMMUNITY HOSPITAL — ROCHESTER

Births	1955 through 1964	Total:	7,285
Therapeutic abortions	1955 through 1964	Total:	1

Ratio: 1:7285

Year	Indications	Committee Rules
1955 through 1964	Adenocarcinoma right breast.	Information not given.

RIVERVIEW MEMORIAL HOSPITAL — ST. PAUL

Births	1955 through 1964	Total:	4,486
Therapeutic abortions	1955 through 1964	Total:	0
Committee Rules	There is no Therapeutic Abortion Board.		

SAINT BARNABAS HOSPITAL — MINNEAPOLIS

Births	1955 through 1964	Total:	21,557
Therapeutic abortions	1955 through 1964	Total:	0
Committee Rules	If abortion is indicated, consultation with 2 other physicians is required. A majority vote rules.		

ST. JOHN'S HOSPITAL — ST. PAUL

Births	1955 through 1964	Total:	20,599
Therapeutic abortions	1955 through 1964	Total:	0
Committee Rules	There is no Therapeutic Abortion Board.		

ST. MARY'S HOSPITAL — DULUTH

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	1,364	1,388	1,574	1,681	1,861	1,920	1,935	1,987	1,918	1,790
Therapeutic abortions	0	0	0	0	0	0	0	0	0	0
Committee Rules	There is no Therapeutic Abortion Board.									

Total births: 17,418

ST. MARY'S HOSPITAL — MINNEAPOLIS

Births	1955 through 1964	Total:	44,901
Therapeutic abortions		Total:	0
Committee Rules	There is no Therapeutic Abortion Board.		

Continued

MORTALITY STUDY

ST. LUKE'S HOSPITAL — DULUTH

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	2,101	2,229	1,987	1,808	1,596	1,461	1,394	1,279	1,187	1,110
Therapeutic abortions	1	1	1	1	0	0	3	2	1	1

Ratio: 1:1468 Total live births: 16,152 Therapeutic abortions: 11

Year	Indications	Committee Rules
1955	Horseshoe kidney, bilateral hydronephrosis, stone left kidney lower calyx, chronic urinary tract infection.	The Sterilization and Therapeutic Abortion Committee is composed of the Chief of the Department of Obstetrics and Gynecology with 2 other physicians, plus a fourth consultant if another field is involved.
1956	Chronic glomerulonephritis, hypertension, early uremia.	
1957	Inactive rheumatic heart disease, cardiac enlargement, mitral stenosis with insufficiency.	
1958	Chronic hemolytic anemia.	
1961	Depressive and anxiety reaction (rape case).	
1961	Ulcerative colitis, anemia secondary severe.	
1961	Polycystic kidneys, hypertension, urinary insufficiency.	
1962	Lupus erythematosus.	
1962	Depressive reaction with suicidal potential	
1963	Severe hypertension, pre-eclampsia, hyperemesis gravidarum.	
1964	Ulcerative colitis, severe anxiety tension state.	

ST. LUKE'S HOSPITAL — ST. PAUL

	1955	1956	1957	1958	1959	1960	1961	1962	1963	1964
Births	1,201	1,218	1,290	1,367	1,302	1,235	1,113	1,005	940	926
Therapeutic abortions			1955 through 1964				Total: 1			

Ratio: 1:11597 Total live births: 11,597 Therapeutic abortions: 1

Year	Indications	Committee Rules
1955 through 1964	No information given on indication.	A consultation with another qualified physician is necessary for a Therapeutic Abortion.

SWEDISH HOSPITAL — MINNEAPOLIS

Births	1955 through 1964	Total: 35,528
Therapeutic abortions	1955 through 1964	Total: 2

Ratio: 1:17764

Year	Indications	Committee Rules
1962	Congenital heart disease, severe.	The committee is composed of 5 members — the Obstetric-Gynecologic, Internal Medicine Urologic and Psychiatric sections of the Medical Staff. A unanimous vote rules.
1963	Chronic glomerulonephritis.	

UNIVERSITY OF MINNESOTA HOSPITAL — MINNEAPOLIS

Births	1955 through 1964	Total: 9,500
Therapeutic abortions	1955 through 1964	Total: 0
Committee Rules	Information not given.	

Medical Poll of Desired Indications for Therapeutic Abortion

Questionnaire

In this analysis, the answers were recorded as "Yes" or "No" when a definite opinion was given. There was a third group tabulated as "Unanswered." In this third group the question was left blank; the person stated he would have to have more information to answer the question, or the answer was so qualified that it meant nothing definitely either for or against the procedure.

Of the two hundred (200) votes returned, one hundred six (106) were from psychiatrists and ninety-four (94) from obstetricians.

There were eight (8) of the 106 psychiatrists or 7.5% that voted straight "Yes" and two (2) of the 94 obstetricians or 2.1% that voted a straight "Yes" for liberalizing all of the indications given for therapeutic abortion.

Ten (10) of the 106 psychiatrists or 9.4% voted a straight "No" and fourteen (14) of the 94 obstetricians or 14.8% voted a straight "No" ballot. They would not do any therapeutic abortions. One of this group, however, stated that he would suggest that the patient see another doctor in any of the given circumstances, if the patient so desired.

There were eighty-eight (88) of the 106 psychiatrists or 83.0% and seventy-eight (78) of the 94 obstetricians or 82.9% that were in favor of liberalization of some of the indications for doing therapeutic abortions.

Questionnaire

These figures and percentages are divided into — (1) Obstetricians and (2) Psychiatrists.

Do You Believe A Pregnancy Should Be Interrupted:

- | | | |
|---|-------------|-------------------|
| I. When the life of the mother is in danger? | | |
| 1) Yes 77-81.9% | No 15-15.9% | Unanswered 2-2.1% |
| 2) Yes 93-87.7% | No 12-11.3% | Unanswered 1-0.9% |
| II. When the physical health of the mother might be impaired? | | |
| 1) Yes 54-57.4% | No 35-37.1% | Unanswered 5-5.3% |
| 2) Yes 72-67.9% | No 27-25.4% | Unanswered 7-6.6% |
| III. When there is significant risk that the mental or emotional health of the mother might be jeopardized? | | |
| 1) Yes 44-46.8% | No 45-47.8% | Unanswered 5-5.3% |
| 2) Yes 75-70.7% | No 28-26.4% | Unanswered 3-2.8% |
| IV. When there is significant risk that the child would be born mentally or physically defective? | | |
| 1) Yes 51-54.2% | No 38-40.4% | Unanswered 5-5.3% |
| 2) Yes 79-74.5% | No 25-23.5% | Unanswered 2-1.8% |
| V. When the pregnancy resulted from rape or incest of a girl under 16? | | |
| 1) Yes 63-67.0% | No 28-29.7% | Unanswered 3-3.1% |
| 2) Yes 84-79.2% | No 19-17.9% | Unanswered 3-2.8% |
| VI. When the pregnancy resulted from rape or incest of a girl over 16? | | |
| 1) Yes 50-53.1% | No 41-53.6% | Unanswered 3-3.1% |
| 2) Yes 70-66.0% | No 30-28.3% | Unanswered 6-5.6% |
| VII. Whenever the woman requests it? | | |
| 1) Yes 1- 1.1% | No 90-95.7% | Unanswered 3-3.1% |
| 2) Yes 8- 7.5% | No 95-89.6% | Unanswered 3-2.8% |

Continued

MORTALITY STUDY

VIII. When a girl under 14 is pregnant?

1) Yes 26-27.6%	No 63-67.0%	Unanswered 5-5.3%
2) Yes 63-59.4%	No 37-34.5%	Unanswered 6-5.6%

Voted straight yes — 1) 2-2.1%
2) 8-7.5%

Voted straight no — 1) 14-14.8%
2) 10-9.4%

Voted for liberalization of some of the indications — 1) 78-82.9%
2) 88-83.0%

Religion of the Physicians

Religion was listed as given by the physician. If this space was left blank or if a statement was recorded such as "Not Pertinent," the religion was listed as "Not given."

Catholic	Non-Catholic	Not Given
13 Obstetricians	75 Obstetricians	6 Obstetricians
14 Psychiatrists	72 Psychiatrists	20 Psychiatrists

The Minnesota Obstetrical and Gynecological Society

The Minnesota Obstetrical-Gynecological Society, at their recent meeting, held December 3, 1966, in Minneapolis, Minnesota, decided to inform the Council of the Minnesota State Medical Association and the appropriate Legislative Committee the results of a post card poll of its members on "Therapeutic Abortion."

The post card poll gave the members three choices:

1. Favor the present Minnesota Statute on "Therapeutic Abortion."*
2. Favor the Model Penal Code of 1959.*
3. Favor some changes, but not Penal Code of 1959.

Out of 157 cards sent, 104 cards were returned, 23 favoring the present statute; 66 favoring the Penal Code of 1959; 15 favoring the third choice.

The Society preferred to take no official action as representing the Society.

*See page 48.

St. Luke's Hospital Seminar

St. Luke's Hospital, St. Paul, is presenting a seminar entitled "Clinical Aspects of Hematology" on April 27, 1967, starting at 1:30 p.m. in the St. Luke's Hospital auditorium. The featured speaker will be Dr. A. J. Quick of Marquette University Medical School. Contact: C. E. Turbak, M.D. at St. Luke's Hospital.



Meetings and Announcements

The discipline which corrects the baseness of worldly passions, fortifies the heart with virtuous principles, enlightens the mind with useful knowledge, and furnishes it with enjoyment from within itself, is of more consequence to real felicity, than all the provisions we can make of the goods of fortune. — Blair

JANUARY

- Southwestern Minnesota Medical Society — January 2, Worthington, 7 p.m.
 Zumbro Valley Medical Society — January 4, Mann Hall, Rochester, 8:00 p.m.
 Brown County Medical Society — January 10, Orchid Inn, Sleepy Eye, 7:00 p.m.
 Minnesota Academy of Medicine — January 11, Town & Country Club, St. Paul, 6:30 p.m.
 Camp Release District Medical Society — January 12, Hunt Hotel, Montevideo, 6:30 p.m.
 St. Louis County Medical Society — January 12, Ex. Comm. at 6:00 p.m.; annual business meeting at 8:00 p.m., St. Mary's Hospital, Duluth.
 Blue Earth Valley Medical Society — January 18, Interlaken Golf Club, Fairmont.
 Twin City Urological Society — January 20, 6:00 p.m.
 Range Medical Society — January 24, Ex. Comm. & annual meeting; 7:00 p.m. dinner, meeting follows, Hibbing.
 National Winter Sports Injury Conference — January 27-29, University of Wisconsin Medical School, Wisconsin Center, Madison, Wisconsin.
 Ramsey County Medical Society — 8:00 p.m. — January 30, 15th floor, Lowry Medical Arts Bldg., St. Paul.
 Big Mountain Medical-Ski Conference, Whitefish, Montana, January 25, 26, 27. Contact: R. D. Buchanan, M.D., Box 220, Columbia Falls, Montana. AAGP Credit 6½ hours. Registration fee: \$5.00.

FEBRUARY

- Southwestern Minnesota Medical Society — February 6, Worthington, 7:00 p.m.
 Nicollet-LeSueur County Medical Society — February 6, Holiday House, St. Peter, 6:30 p.m.
 Scott-Carver County Medical Society — February 7.
 St. Louis Co. Med. Society — St. Lukes, Duluth — February 9, (Ex. Comm. at 6:00 p.m. Regular meeting at 8.)
 Minnesota Academy of Medicine — February 8, Town & Country Club, St. Paul, 6:30 p.m.

- Camp Release District Medical Society — February 10, Hunt Hotel, Montevideo.
 Wisconsin Academy of General Practice — February 14-16, Mt. Telemark Ski Conference, Cable, Wisconsin.
 Blue Earth Valley Medical Society — February 15, Interlaken Golf Club, Fairmont.
 Minnesota Academy of Occupational Medicine and Surgery — February 16, Minneapolis Club, 6:30 p.m.
 Twin City Urological Society — February 17, 6:00 p.m.
 Hennepin County Academy of General Practice — February 20, Athletic Club, Minneapolis, 6:00 p.m.
 Ramsey County Medical Society — February 27, 15th floor, Lowry Medical Arts Bldg., St. Paul, 8:00 p.m.

MARCH

- Northwestern Pediatric Society — March-Spring meeting to be set.
 Zumbro Valley Medical Society — March 1, Mann Hall, Rochester, 8:00 p.m.
 Southwestern Minnesota Medical Society — March 6, Worthington, 7:00 p.m.
 Hennepin County Medical Society and Hennepin County Academy of General Practice — March 6, Pick-Nicollet Hotel, Minneapolis, 6:00 p.m.
 Scott-Carver County Medical Society — March 7,
 Minnesota Academy of Medicine — March 8, Town & Country Club, St. Paul, 6:30 p.m.
 St. Louis County Medical Society — March 9, Ex. Comm. at 6:00 p.m., regular meeting at 8:00 p.m., St. Mary's Hospital, Duluth.
 Camp Release District Medical Society — March 10, Hunt Hotel, Montevideo.
 Blue Earth Valley Medical Society — March 15, Interlaken Golf Club, Fairmont.
 Twin City Urological Society — March 17, 6:00 p.m.
 Hennepin County Academy of General Practice — March 20, Athletic Club, Minneapolis, 6:00 p.m.
 Ramsey County Medical Society — 8:00 p.m. — March 27, 15th floor, Lowry Medical Arts Bldg., St. Paul.
 Range Medical Society — March 28, Ex. & General Mtg., dinner at 7:00 p.m., Hibbing.

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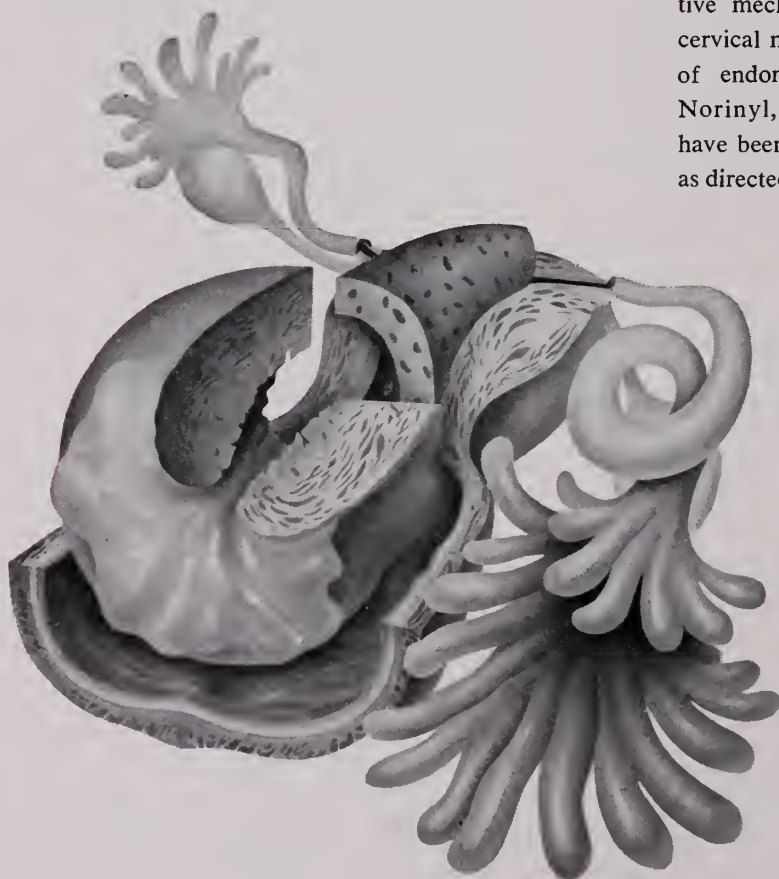
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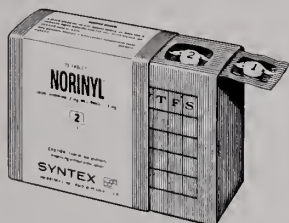
plus important supportive benefits that help her through those critical early months of oral contraception

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Contraindications: Thrombophlebitis or pulmonary embolism (current or past). Existing evidence does not support a causal relationship between use of Norinyl and development of thromboembolism. While a study which was conducted does not resolve definitively the possible etiologic relationship between progestational agents and intravascular clotting, it tends to con-

firm the findings of the Ad Hoc Advisory Committee appointed by the Food and Drug Administration to review this possibility. Cardiac, renal or hepatic dysfunction. Carcinoma of the breast or genital tract. Patients with a history of psychic depression should be carefully studied and the drug discontinued if depression recurs to marked degree. Patients with a history of cerebral vascular accident.

Warning: Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn.

Precautions: By May 1963, experience with norethindrone 2 mg.—mestranol 0.1 mg. had extended over 24 months. Through miscalculation, omission or error in taking the recommended dosage of Norinyl, pregnancy may result. If regular menses fail to appear and treatment schedule has not been adhered to, or if patient misses two menstrual periods, possibility of pregnancy should be resolved before resuming Norinyl. If pregnancy is established, Norinyl should be discontinued during period of gestation since virilization of the female fetus has been reported with oral use of progestational agents or estrogen. When lactation is desired, withhold Norinyl until nursing needs are established. Existing uterine fibroids may increase in size. In metabolic or endocrine disorders, careful clinical preevaluation is indicated. A few patients without evidence of hyperthyroidism had elevated serum protein-bound iodine levels, which in the light of present knowledge, does not necessarily imply hyperthyroidism. Protein-bound iodine increased following estrogen administration. Bromsulphalein retention has occurred in up to 25% of patients without evidence of hepatic dysfunction. Studies from 24-hour urine collections have shown an increase in aldosterone and 17-

ketosteroids and decrease in 17-hydroxycorticoid levels. Thus, Norinyl should be discontinued prior to and during thyroid, liver or adrenal function tests. Because progestational agents may cause fluid retention, conditions such as epilepsy, migraine and asthma require careful observation. Thus far no deleterious effect on pituitary, ovarian or adrenal function has been noted; however, long-range possible effect on these and other organs must await more prolonged observation. Norinyl should be used with caution in patients with bone, renal or any disease involving calcium or phosphorus metabolism. **Side Effects:** Intermenstrual bleeding; amenorrhea; symptoms resembling early pregnancy, such as nausea, breast engorgement or enlargement, chloasma and minor degree of fluid retention (if these should occur and patient has not strictly adhered to medication plan, she should be tested for pregnancy); weight gain; subjective complaints such as headache, dizziness, nervousness, irritability; in a few patients libido was increased. In a total of 3,090 patients, 2.2% discontinued medication because of nausea.

NOTE: See sections on contraindications and precautions for possible side effects on other organ systems.

Dosage and Administration: One Norinyl tablet orally for 20 days, commencing on day 5 through and including day 24 of the menstrual cycle. (Day 1 is the first day of menstrual bleeding.)

Availability: Dispensers of 20 and 60 tablets; bottles of 100.

References: 1. Council on Drugs. JAMA 187:664 (Feb. 29) 1964. 2. Brvans, F. E.: Canad Med Ass J 92:287 (Feb. 6) 1965. 3. Goldzieher, J. W.: Med Clin N Amer 48:529 (Mar.) 1964. 4. Cohen, M. R.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965. 5. Hammond, D. O.: Ibid. 6. Rice-Wray, E., Goldzieher, J. W., and Aranda-Rosell, A.: Fertil Steril 14:402 (Jul.-Aug.) 1963. 7. Goldzieher, J. W., Moses, L. E., and Ellis, L. T.: JAMA 180:359 (May 5) 1962. 8. Kempers, R. D.: GP 29:88 (Jan.) 1964. 9. Tyler, E. T.: JAMA 187:562 (Feb. 22) 1964. 10. Rudel, H. W., Martinez-Manautou, J., and Maqueo-Topete, M.: Fertil Steril 16:158 (Mar.-Apr.) 1965. 11. Flowers, C. E., Jr.: N Carolina Med J 25:139 (Apr.) 1964. 12. Goldzieher, J. W.: Appl Ther 6:503 (June) 1964. 13. The Control of Fertility. Report adopted by the Committee on Human Reproduction of the American Medical Association. JAMA 194:462 (Oct. 25) 1965. 14. Flowers, C. E., Jr.: JAMA 188:1115 (June 29) 1964. 15. Merritt, R. I.: Appl Ther 6:427 (May) 1964. 16. Newland, D. O.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965.

norethindrone—an original steroid from
SYNTEX
LABORATORIES INC., PALO ALTO, CALIF.

Norinyl tablets
(norethindrone 2 mg $\bar{c}$ mestranol 0.1 mg)

for multiple contraceptive action



Now, now, Mrs. Forsythe, we've never lost a cold patient yet.

When she's experiencing acute discomfort from cold symptoms, it's small wonder the patient becomes distressed about her condition.

She will breathe easier when you prescribe Novahistine LP.

Novahistine LP is a long-acting decongestant that helps restore normal mucus secretion and ciliary activity—physiologic mechanisms which prevent infection of the respiratory tract. A dose of two tablets taken in the morning and repeated in the evening will usually keep air passages clear for 24 hours.

Use cautiously in individuals with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Caution patients who operate machinery or motor vehicles that drowsiness may result.

Each Novahistine LP tablet contains: phenylephrine hydrochloride, 25 mg., and chlorpheniramine maleate, 4 mg.

 **PITMAN-MOORE** Division of The Dow Chemical Company, Indianapolis

NOVAHISTINE[®] LP

For relief of nasal congestion.

Saxon

Your Bank Accounts

IN OUR BUSINESS, it is fairly common for us to find clients with large accumulations of money in checking, savings, and saving or building and loan accounts. Quite frequently, there are sound investment reasons for our recommending substantial transfer to other mediums.

This recommendation is especially valid for checking accounts which provide no yield whatsoever. Every \$1,000 of excess checking balance costs its owner at least \$40 annually in sacrificed earnings. In the case of savings accounts, we must determine whether an imbalance exists between fixed dollars and variable commitments, before recommending transfers of large sums.

Recent embezzlements, by bank employees in the Midwest, of very substantial sums have highlighted another reason for limiting the funds in a bank account. This reason is simply excess risk exposure.

By far the most outstanding example of this risk exposure is the recent embezzlement of over \$2 million by a trusted employee and stockholder in a Sheldon, Iowa bank. This defalcation has directly or indirectly contributed to the complete insolvency of the bank, bankruptcy of one of the leading industries in that town and the threat of crippling losses to numerous persons with over \$15,000 on deposit with that bank.

If you carry more than \$15,000 in a bank account,

you also may be unduly exposed to such a loss, and it's too late after you read about the embezzlement in your local paper. If investment logic alone does not dictate limitations on your bank accounts, certainly safety factors do.

The Federal Deposit Insurance Corporation and the Federal Savings and Loan Insurance Corporation provide full protection on bank and savings and loan accounts up to \$15,000. This \$15,000 is *per entity*, that is the individual, joint, partnership or corporate account.

In the case of a husband and wife, it would be possible for them to be fully insured on \$45,000 of deposits in one bank — if the accounts are properly designated. The husband can have \$15,000 in his name, the wife \$15,000 in hers, and an additional \$15,000 will be insured in a joint account. *Two* accounts in the *same name* are insured only once — for \$15,000.

Beyond this \$45,000 level, husband and wife should place their funds in a second bank or savings and loan organization. Above all, money should never be deposited with an institution not participating in the Federal insurance program.

If you are carrying excess funds in your checking or savings account, you have a two-fold interest in reducing them. Both investment principles and safety reasons dictate a revision of these accounts.

William D. Huntington*
Minneapolis, Minnesota

*Northern Division Manager, Professional Management Midwest.

Minnesota State Board of Medical Examiners

The Minnesota State Board of Medical Examiners and the State Examining Committee for Physical Therapists have announced that persons desiring to take the examination for registration of physical therapists must be graduates of a school of physical therapy approved by the Board for training physical therapists, in addition to the other statutory qualifications. Persons interested in determining their eligibility to take the examination for registration in physical therapy are advised to contact the Board in order to insure that the school they propose to attend is one approved by the Board.

Minnesota Obstetrical-Gynecological Society

The next meeting of the Minnesota Obstetrical-Gynecological Society will be held in Duluth, April 29th. The following doctors will be the guest speakers:

Howard Jones, M.D. — subject to be announced

Georgianna Jones, M.D. — Role of Estrogens in the Aging Female

The Doctors Jones are husband and wife and are from the Johns Hopkins Hospital in Baltimore.

Contact: Theodore Watson, M.D., 1261 Lowry Medical Arts Building, St. Paul.



Physician's Diary

When a great merchant of Liverpool was asked by what means he had contrived to realize the large fortune he possessed, his reply was, "By one article alone, in which thou mayest deal too, if you pleasest — it is civility." — Bentley

NEW LOCATIONS: Dr. Arlo Pitcher is the new physician in St. James . . . Dr. William D. Brown, Jr. has opened up new offices in Minneapolis . . . Doctors Mustafa Vidinli and Wilfred Pinsonneault have joined the Delmore Clinic in Roseau . . . Dr. J. E. Nord has begun a practice at the Hawley Medical Center in Hawley . . . Dr. Andrew Steiner has left St. Michael to open up a practice in Minneapolis. Dr. Nick Koropchak has joined the staff of the Fridley Medical Center in Fridley.

* * *

Dr. Jesse E. Edwards, Charles T. Miller Hospital, St. Paul, is the newly elected president of the American Heart Association.

* * *

Dr. C. G. Uhley has retired from the staff of the Northwestern Clinic in Crookston after almost thirty years of association. He and Mrs. Uhley intend to spend their retirement in Palm Desert, California.

* * *

Dr. O. J. Swenson of Waseca was honored by that community on occasion of his 40th year in the practice of medicine in Waseca. An open house reception was held.

* * *

Dr. D. B. Soriano, recently on the staff of the Willmar State Hospital, has joined Doctors G. T. Midboe, J. L. Purdie, C. F. Peikert at the Doctors Clinic in Forest Lake.

* * *

Dr. Tague Chisholm is the new president of the Hennepin County Medical Society, and Dr. James C. Mankey is the secretary.

* * *

Dr. Malcolm Campbell, Rochester, was elected president of the Zumbro Valley Medical Society. Other newly elected officers were: Dr. David Utz, vice president, and Dr. Martin Van Herik, secretary-treasurer, both of the Mayo Clinic.

* * *

Dr. O. K. Behr was elected chief-of-staff and president of the Medical Staff at Bethesda Hospital in Crookston at its annual meeting in November. Dr. J. S. Rubin was elected vice president, and Dr. Robert Schnable, secretary.

* * *

Dr. Robert A. Ulstrom, chairman of the pediatrics

department of the Center for Health Sciences at the University of California, has been named associate dean of the College of Medical Sciences at the University of Minnesota. He assumed his new post December 1st.

* * *

Dr. Samuel M. Reichel, Minneapolis, presented a paper at the annual meeting of the American Association for Automotive Medicine at Holloman Air Force Base, Alamogordo, New Mexico in November. The title of the paper was "Moderate Auto Injuries: The Role of Reflexes in Pathogenesis and Symptomatology."

* * *

Dr. George B. Logan, a member of the Section of Pediatrics of the Mayo Clinic, was chosen president-elect of the American Academy of Pediatrics at the annual meeting of the organization in October.

* * *

Dr. Laurentius O. Underdahl, head of a section of medicine at the Mayo Clinic, was inducted as president of the Minnesota Society of Internal Medicine at its annual meeting in October, and Dr. John A. Spittell, Jr., head of a section of medicine in the Mayo Clinic, was elected secretary-treasurer.

* * *

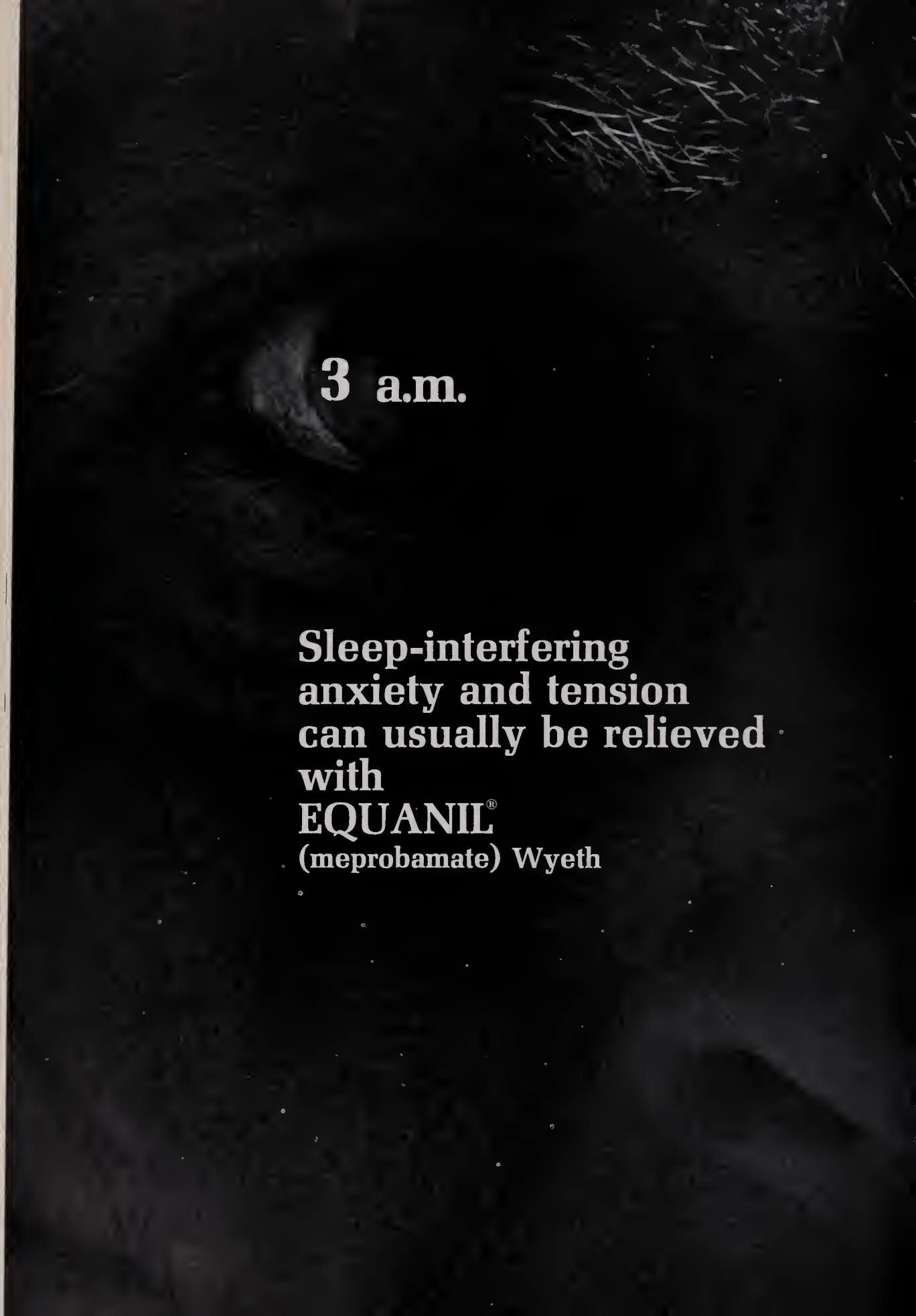
Dr. Karl W. Anderson, retired vice-president and medical director of Northwestern National Life Insurance Company in Minneapolis, has been elected president of the Minnesota Medical Foundation. Dr. N. L. Gault, Jr., associate dean of the University of Minnesota College of Medical Sciences, was re-elected secretary-treasurer.

* * *

Dr. Howard Polley, Mayo Clinic specialist in rheumatic diseases, was elected vice president of the Arthritis Foundation at its annual meeting in November, and Dr. Arthur Bulbulian, emeritus member of the Mayo Clinic staff, has been re-elected editor of the American Academy of Maxillofacial Prosthetics.

* * *

Dr. Wendell Hall, professor, Department of Internal Medicine, University of Minnesota School of Medicine, and on the staff of the Veterans Administration Hospital, received an unrestricted grant for medical research from Wyeth Laboratories.



3 a.m.

**Sleep-interfering
anxiety and tension
can usually be relieved
with
EQUANIL[®]
(meprobamate) Wyeth**



Cautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use may result in dependence or habituation in susceptible persons—as ex-addicts, alcoholics, severe psychoneurotics. After prolonged high dosage, drug should be withdrawn gradually to avoid possibly severe withdrawal reactions including epileptiform seizures. Side effects include drowsiness and, rarely, allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute non-thrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. Meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Warn patients of possible reduced alcohol tolerance. Should drowsiness, ataxia, or visual disturbances occur, dose should be reduced. If symptoms persist, patients should not operate vehicles or dangerous machinery. A few cases of leukopenia, usually transient, have been reported following prolonged dosage. Other blood dyscrasias—aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia—have occurred rarely, almost always in the presence of known toxic agents. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. Prescribe very cautiously for patients with suicidal tendencies. Suicidal attempts should be treated with immediate gastric lavage and appropriate supportive therapy.

Contraindications: History of sensitivity to meprobamate.

Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

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Philadelphia, Pa.





fluocinolone acetonide — an original steroid from

SYNTEX 

LABORATORIES INC., PALO ALTO, CALIF.

controls infected inflammatory dermatoses that start from scratch



Neo-Synalar®
fluocinolone acetonide-neomycin sulfate cream)
Cream

The "itch-scratch" cycle usually associated with inflammation often results in infected dermatoses because broken skin surfaces are particularly vulnerable to pathogenic bacteria.¹ To treat infected inflammatory dermatoses, Neo-Synalar Cream combines the most active topical corticosteroid with a highly reliable antibiotic generally reserved for topical application.

In Neo-Synalar, fluocinolone acetonide controls the inflammation and provides rapid relief from associated pruritus. At the same time, its antibacterial component—neomycin—combats superficial infection caused by many gram-positive and gram-negative bacilli² that often colonize and thrive on abraded skin.¹

A specially formulated vanishing cream base that is greaseless and odor free makes Neo-Synalar cosmetically appealing, and encourages greater patient cooperation.

controls the infection

stops the scratch

Contraindications: Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of its components. **Precautions:** Neomycin rarely produces allergic reactions. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. **Side Effects:** Side effects are not ordinarily encountered with topical corticosteroids. As with all drugs, however, a few patients may react unfavorably to Neo-Synalar under certain conditions. **Availability:** Neo-Synalar Cream (0.025% fluocinolone acetonide, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes.

References: 1. Pillsbury, D. M., Shelley, W. B., and Kligman, A. M.: A manual of cutaneous medicine, Philadelphia, Saunders, 1961, p. 79. 2. Barber, M., and Garrod, L. P.: Antibiotic and chemotherapy, Baltimore, Williams and Wilkins, 1963, p. 111.

**How long will it take him
to recover from the flu
if he just doesn't care?**



**Does he really care?
Is he alert, encouraged,
positive and optimistic
about getting out of bed
and back to work soon?**

**Or is he giving in to
the depressing impact
of confinement?**

**When functional fatigue
complicates convalescence,
Alertonic can help...**

Pleasant-tasting Alertonic is pipradrol hydrochloride—an effective cerebral stimulant whose gentle analeptic action helps counteract the apathy and inertia that so often delay convalescence—together with an excellent vitamin and mineral formula, in a satisfying 15% alcohol vehicle.

Nothing fosters confidence and a sense of well-being better than your own personal warmth, understanding and encouragement together with Alertonic to help insure prompt response.

Adequate dosage is important: Prescribe Alertonic—one tablespoonful t.i.d., 30 minutes before meals...tastes best chilled.

And for your patient's sake, prescribe Alertonic in the convenient, economical one-pint bottle.

Alertonic®

Available Only On Prescription

Each 45 cc. (3 tablespoonfuls) contains: alcohol, 15%; pipradrol hydrochloride, 2 mg.; thiamine hydrochloride (vitamin B₁) (10 MDR*), 10 mg.; riboflavin (vitamin B₂) (4 MDR), 5 mg.; pyridoxine hydrochloride (vitamin B₆), 1 mg.; niacinamide (5 MDR), 50 mg.; choline,† 100 mg.; inositol,† 100 mg.; calcium glycerophosphate, 100 mg. (supplies 2% MDR for calcium and for phosphorus) and 1 mg. each of the following: cobalt (as chloride), manganese (as sulfate), magnesium (as acetate), zinc (as acetate), and molybdenum (as ammonium molybdate).

*Multiple of adult Minimum Daily Requirement supplied.

†The need for these substances in human nutrition has not been established.

Indications: 1. Functional fatigue such as that often associated with: a depressing life experience or stressful time of life; advancing years; convalescence; limited activity or confinement. 2. Poor appetite and vitamin-mineral deficiency as they occur in: patients having faulty eating habits; geriatric patients who are losing interest in food; patients convalescing from debilitating illness or surgery.

Contraindications: As with other drugs with CNS stimulating action, Alertonic is contraindicated in hyperactive, agitated or severely anxious patients and in chorea or obsessive compulsive states.

Side effects: Reports of overstimulation have been rare. Patients who are known to be unduly sensitive to the effects of stimulant drugs should be observed carefully in the initial stages of treatment.

Dosage: Adults, 1 tablespoonful; children (over 15 years old), 1 to 2 teaspoonfuls; children (4 to 15 years old), 1 teaspoonful. To be taken three times daily 30 minutes before meals.

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6-7907

**Os
frontale**

**Sinus
frontalis**

**Crista
galli**

**Os
nasale**

Lamina cribrosa ossis ethmoidalis

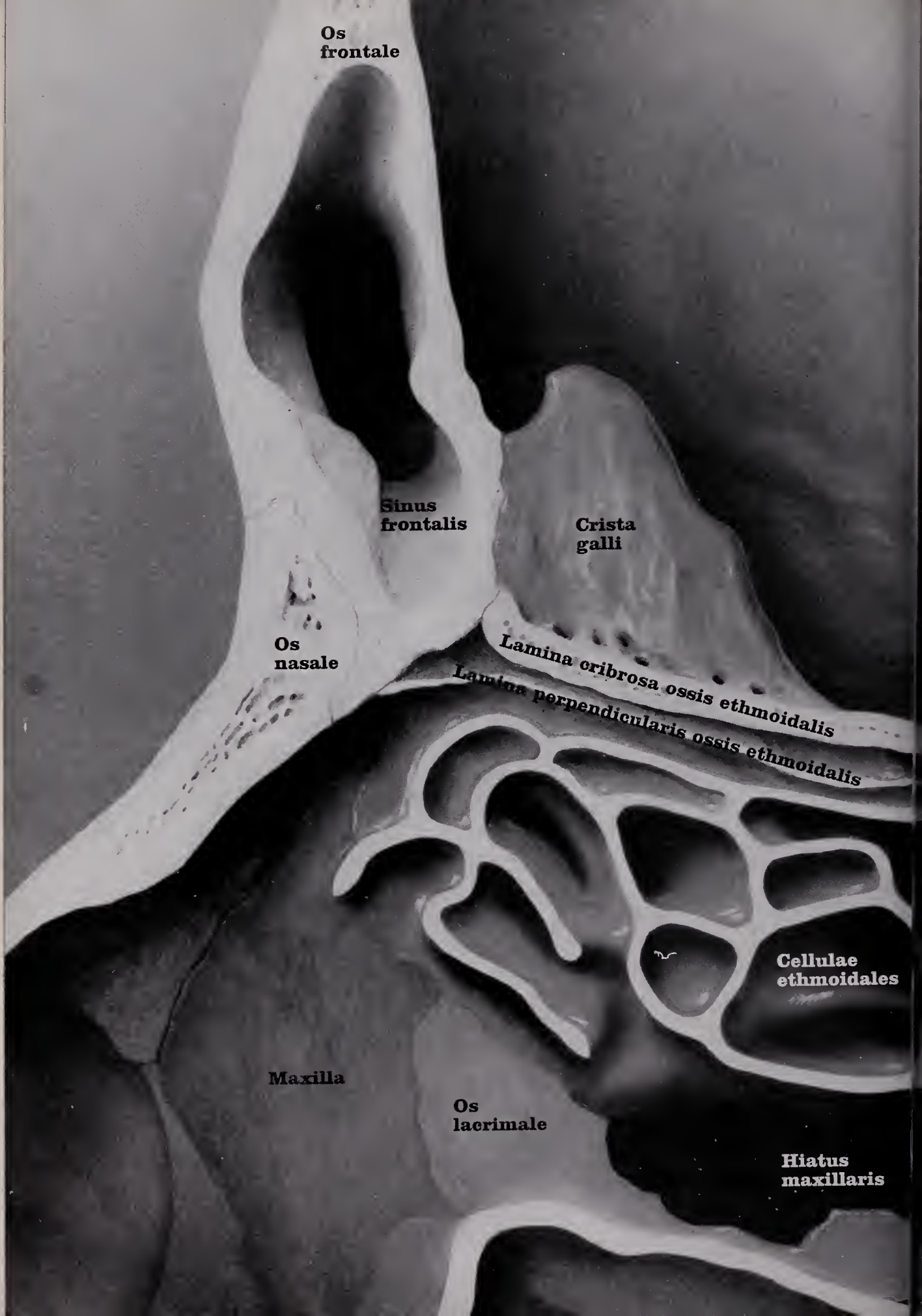
Lamina perpendicularis ossis ethmoidalis

**Cellulae
ethmoidales**

Maxilla

**Os
lacrimale**

**Hiatus
maxillaris**



Sinus headache is not a single entity,
but a chain reaction of pain.
It is facial pain—deep, dull, aching and
nonpulsating. It is referred pain—
originating in the nose and sinuses but
felt at another site. It may become
generalized pain and tension in head and
neck. It is one or all of these.

The Sinutab formula is designed
for symptomatic relief of sinus headache.

It provides two analgesics to relieve
pain and discomfort...an effective oral
decongestant to reduce mucosal congestion...
and an antihistamine to help
control allergic manifestations.

Side Effects: Epigastric distress, drowsi-
ness, dizziness, insomnia and nervousness.

Precautions: Instruct patients not to drive
or operate machinery if drowsiness occurs.

Use with caution in patients with thyroid
disease, heart disease, hypertension, diabetes
or kidney disease. Excessive dosage or
prolonged use may cause kidney damage.

Dosage: Adults—2 tablets every 4 hours.

WARNER-CHILCOTT
Morris Plains, N.J.



SINUTAB[®] **for sinus headache**

Each tablet contains
150 mg. acetaminophen,
150 mg. phenacetin,
25 mg. phenylpropanolamine HCl,
and 22 mg. phenyltoloxamine
citrate.

8-OP-71-CC

special formula for a special problem

*specifically formulated
for symptomatic
relief of sinus headache*

**Sinus
sphenoidalis**

**Os
occipitale**

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Classified advertising rates are twenty (20) cents a word; minimum monthly charge \$5.00; key number, fifty (50) cents additional.

Replies to advertisements with key numbers should be mailed in care of MINNESOTA MEDICINE, 496 Lowry Medical Arts Bldg., St. Paul, Minn. 55102

GENERAL PRACTITIONER wanted to join well-established practitioner. New clinic building — 90 miles east of St. Paul — city of 14,000. Early partnership with full hospital facilities. Ideal location. L. W. Picotte, M.D.; Chippewa Falls, Wisconsin.

FOR SALE: Mattern x-ray unit K.V.-60. Good for chest and extremity work. Also an examining table, instrument cabinet, E.K.G., and other equipment. Contact L. A. Whitesell, Jr., M.D. 207 South 1st Street, Buffalo, Minnesota 55313.

INTERNIST for 20-physician-clinic in prosperous Minnesota city. Salary negotiable first year, then full partnership. East Range Clinic, Virginia, Minnesota.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 289; 496 Lowry Medical Arts Building; St. Paul, 55102.

OFFICE SPACE now available in busy Bloomington. 713 square feet of new space in building with busy group of G.P.'s, dentist and suburban OB-GYN office. Ideal for ophthalmology, ENT or pediatrics. 8040 Penn Avenue South. 888-9211.

WANTED — Internist, board certified or qualified, to associate with two board certified internists. Ten man multi-specialty group. (Lenont Peterson Clinic, Virginia, Minnesota) — Heart of the expanding taconite industry.

GENERAL PRACTITIONER, associate, urgently needed. Unopposed practice established 20 years. 32 bed new hospital with additional 20 bed chronic unit. Good anesthesia coverage, lab. facilities. Excellent clinic one block from hospital. Salary with early partnership. Locum tenens also considered. Call collect 218-782-4725 or write Klefstad Clinic, Greenbush, Minnesota.

WANTED: GP to join clinic serving population area of 12,000. City has new hospital, new clinic building, two nursing homes, new Jr-Sr high school, new swimming pool, rich farming area in Red River Valley. Fishing and hunting nearby; metropolitan city close by. Salary open and partnership if interested. Write or call Warren Clinic, Warren, Minnesota 742-6231, area code 218.

LARGE GROUP WITH OFFICES IN TWO CITIES is looking for General Practitioner to add to a two-man general practice clinic. Practice limited only by your abilities and interests with ready consultation from specialty partners in other office located in adjacent city. Full partnership after first year. Write: MINNESOTA MEDICINE — 358; 496 Lowry Medical Arts Building, St. Paul, 55102.

GENERAL PRACTITIONER WANTED for small town practice with two other general practitioners. Practice to include surgery and obstetrics within your own capabilities. Eligible for partnership after first year. Write: MINNESOTA MEDICINE — 359; 496 Lowry Medical Arts Building, St. Paul 55102.

THREE MAN group in North West Wisconsin Resort, State Conservation and Retirement Area needs two more physicians adequately to serve their practice. Facilities offered are three-room physician suites, X-ray and lab under AMT technician, RN-only nursing personnel. New accredited thirty-two bed hospital and forty-six bed nursing home. Deer and duck hunting, fishing within five minutes of town. Internist most needed; generalists welcomed. Will meet any reasonable salary request. Partnership after one year. Write: MINNESOTA MEDICINE — 365; 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED: young internist and pediatrician, board certified or eligible, to join five-man group consisting of three GPs, a general surgeon and a radiologist. College town serving population of 22,000 thirty miles from Twin Cities. Salary open with early partnership opportunity. Write or call collect: Ed Jenkins, Manager, River Falls Medical Clinic, River Falls, Wisc. Phone 425-5322.

GENERAL SURGEON — Board certified experienced, all phases surgery and general practice. Prefer Twin Cities area. Write: MINNESOTA MEDICINE — 367; 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED: Young general practitioner to join five-man group consisting of three GPs, a general surgeon, and radiologist. College town serving population of 22,000 30 miles from Twin Cities. Also need LOCUM TENENS in general practice. Contact: Ed Jenkins, Manager, River Falls Medical Clinic, River Falls, Wisconsin, Phone 425-5322.

PSYCHIATRIST (or interest in psychiatry) and general physician. 1,300 bed NP hospital with progressive treatment, full supporting staff. Community of 35,000 in hunting and fishing area, three colleges, 1½ hours from University of Minnesota. Salary range \$15,000-\$20,000 depending on qualifications. Liberal fringe benefits. Financial assistance in moving. License in one of the States, United States, required. Nondiscrimination in employment. Write Chief-of-Staff, VA Hospital, St. Cloud, MN 56301.

CLINIC BUILDING Morton, 107 W., West St. Paul, located in excellent area. Operated successfully for several years. Partially equipped. This fine building is for SALE or for RENT. For details call Stephen Hofstad, 224-2346 or write: Stephen Hofstad, John E. Blomquist, Inc., 712 N.W. Bank Building, St. Paul.

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DON'T OVERLOOK THIS . . . 3 months' rent free in modern medical clinic — successful location in N.W. suburb of Minneapolis. Come see anytime — 36th and Noble Avenue North. Noble Drug, Ju 8-9449, Ben or Lou.

FOR RENT: Space available for surgical subspecialists. Excellent location. Near Unity Hospital, 10 minutes from Mercy. Share space with General & Thoracic Surgeon and 2 interns. Call Mrs. Winkel — 560-1700, Fridley.

WANTED: General surgeon, qualified or certified. Six man group in Minnesota. Fully accredited 150 bed hospital, open staff. Further information. Write: Falls-Starekow Clinic, Thief River Falls, Minnesota.

IMMEDIATE OPENINGS for full-time or part time **PHYSICIANS** to staff the University Health Service. Good opportunity for semi-retired M.D. Limited call duty. Professional qualifications with first correspondence. Contact Director: K. L. Nelson, M.D., Texas A&M University Hospital, College Station, Texas 77841. Telephone (AC 713-846-4704).

FOR LEASE IN TWIN CITIES — small clinic, large parking area. With lease goes incredibly lucrative general practice, patients' records and excellent staff, at **NO FEE**. Write: **MINNESOTA MEDICINE — 371; 496 Lowry Medical Arts Building, St. Paul 55102.**

INTERNIST AND GENERAL PRACTITIONER wanted to join a four-man clinic group in suburban Minneapolis. Laboratory and X-ray with part-time radiologist. Excellent open hospital staff association. Salary to start with early partnership. Write: **MINNESOTA MEDICINE — 372; 496 Lowry Medical Arts Bldg., St. Paul 55102.**

RESIDENCIES IN PHYSICAL MEDICINE and Rehabilitation offer challenge and opportunity in a growing field. Comprehensive training utilizing Mayo Clinic facilities and faculty, at \$3600 to \$10,000 stipend. Attractive community, excellent school system, cultural advantages. Contact Gordon Martin, M.D., Mayo Graduate School of Medicine, Rochester, 55901.

REALLY LIVE — ON THE ST. CROIX. Your own retreat. Nearer skiing — dock your boat. Spring Company has several. Contact: Harold Onstad, Marine on St. Croix. Call 663-8261.

WANTED: Locum tenens for large general practice St. Paul, Minnesota for February 1967. Salary open. Write: **MINNESOTA MEDICINE — 369, 496 Lowry Medical Arts Building, St. Paul 55102.**

GENERAL PRACTITIONER needed to take over my very active practice on or before June 1, 1967. All equipment nearly new. Records extremely complete. Contact: Gerald E. Cotton, M.D., Fosston, Minnesota.

MINNESOTA MEDICINE Cover Photographs

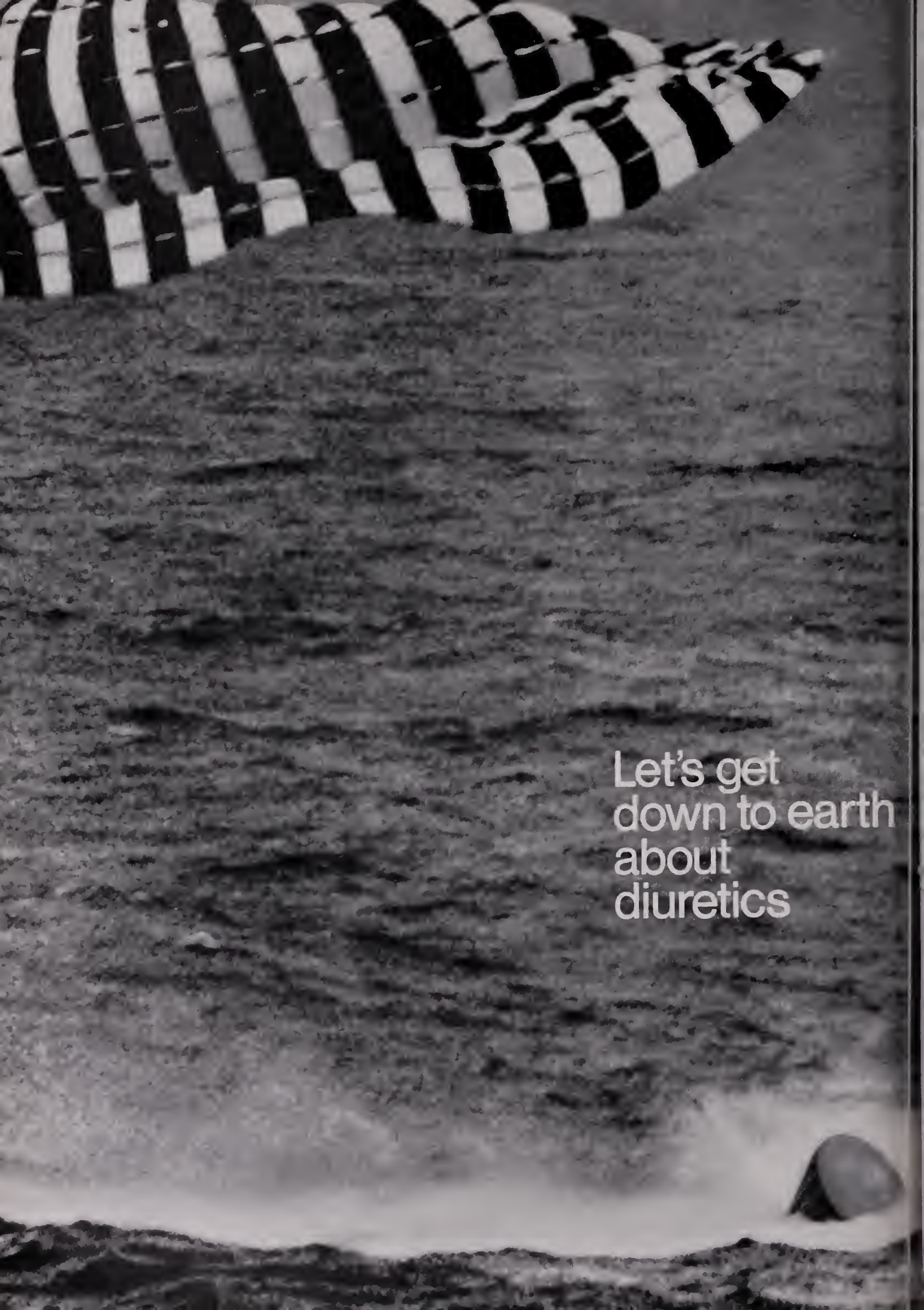
In order to encourage more physicians to submit color slides for use on the cover of **MINNESOTA MEDICINE** the competition is being discontinued. The picture editor now invites all physician-photographers to send 35 mm. color slides of suitable subjects for consideration as cover pictures. The format must be horizontal because of printing limitations. Pictures highlighting Minnesota seasons, places, and activities will have an automatic advantage. No limit as to the number of slides sent will be set, but all slides should be individually identified. All slides will be returned. Physicians whose pictures are used as covers will be recognized in **MINNESOTA MEDICINE**. We can use many more pictures than we have received in the past.

Surgical Meeting

A dinner meeting of the Minneapolis Surgical Society will be held February 2 at the Minneapolis Club in Minneapolis at 6:00. The following speakers will be guests of the Society for that evening:

Donald A. Bolt, M.D. — Trauma in Genesis of Pancreatic Cyst and Pseudo Cyst

David E. Raab, M.D. — Surgical Treatment of Atrial Septal Defect



Let's get
down to earth
about
diuretics

With Hygroton, you'll discover that you can almost always use fewer tablets than is possible with other diuretics.

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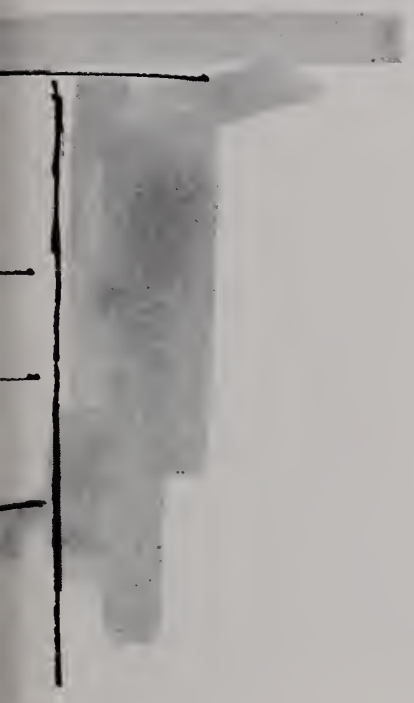
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*Brest, A. N., et al.: J. New Drugs 5:329, 1965.

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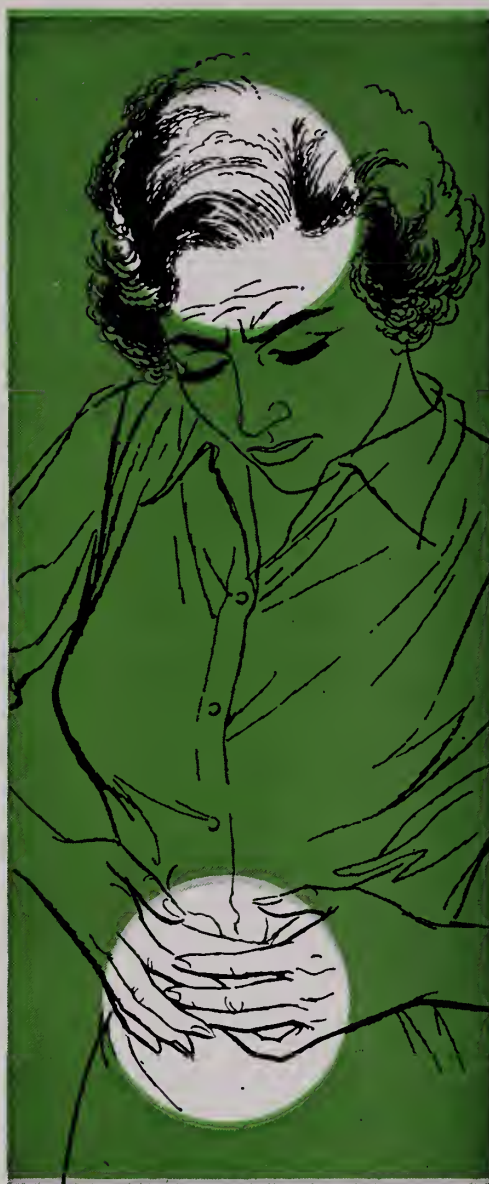
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Minnesota Medicine at a Glance

Corn Allergy — Johnson

Page 35

Of fifty consecutive patients who had food allergies, twenty-five were allergic to corn. According to Dr. K. J. Johnson, corn should be considered one of the most important causes of food allergy. Females seem to have allergies to corn more than males, and most drugs in tablet or capsule form are apt to contain corn.

Cerebral Blood Flow — Meyer and Handa

Page 39

Cerebral blood flow, electroencephalogram, and oxygen consumption were measured in regionally anesthetized, immobilized, and artificially ventilated monkeys. The cerebral venous flow remained unchanged until a temperature of 39-39.4° C. was reached. Thereafter, cerebral venous flow increased to a maximum of 30-50% above steady state values at 41.5-41.9° C. Cerebral metabolic rate for oxygen was also increased significantly (35% on the average) between 40-42° C. When the rectal temperature exceeded 42° C., both cerebral venous outflow and cerebral oxygen metabolism decreased rapidly and the electroencephalogram became abnormal. If hyperthermia was sustained at 41° C., there was a progressive decrease in cerebral venous flow and cerebral oxygen metabolism, and the EEG became progressively abnormal.

Under the conditions used in these experiments, cerebral blood flow and oxygen metabolism remained constant during hyperthermia up to 39° C. Above this level both were increased, and above 42° C. cerebral oxidative metabolism, blood flow, and electroencephalogram failed. Increases in cerebral blood flow and metabolism appear to be relatively smaller than increases of systemic circulation and metabolism reported by others during hyperthermia.

Lacerations of Hand Tendons — Peterson and Lipscomb

Page 101

Lacerations of the tendons of the hands may be complicated and disabling injuries. Successful repair depends on accurate evaluation of the injury, knowledge of the intricate anatomy of the hand, training in the technique of tendon repair, judgment and experience. The authors review the pertinent surgical anatomy of the hand; emphasize the need for proper operating-room conditions for evaluation and treatment; and review the current methods available for successful tendon repair. When conditions are not optimal, and when uncertainty exists as to what to do, it is usually never wrong to perform a toilet and debridement of the wound and close the skin. This will ensure uncomplicated primary healing and enable a successful secondary reconstruction.

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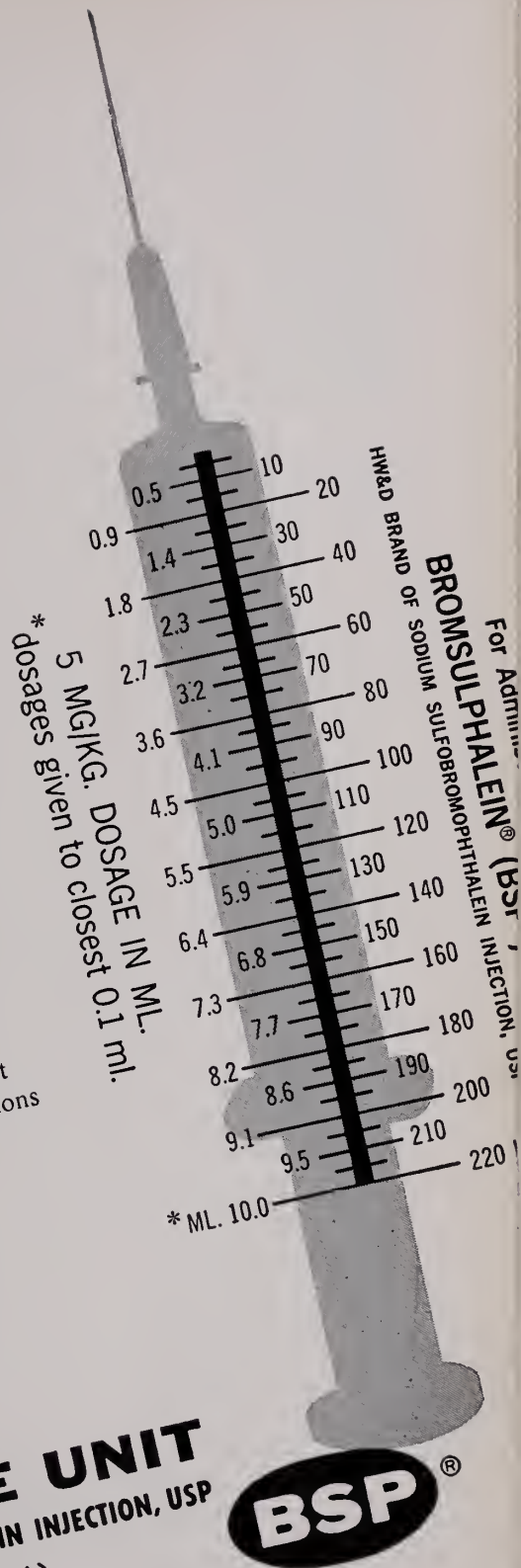
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President's Letter

THIS LETTER will serve both as a warning and as a plea. Some of you who read this message will know all about the story, but the great majority will not have heard it. Please tolerate and read the rather prosaic background information which must be given to you first, in order to get to the punch lines coming later.

Beginning in the winter and spring of 1961-62 a program was started which was entitled the "Minnesota G.P. Psychiatric Training Program." Since that time a total of about 165 physicians have completed the prescribed curriculum. The courses have been splendid "refreshers" in psychiatry given in such a way that all who took them could understand the material, and every effort was made to bring the entire course "close to home" for all participants.

Until July, 1966, these seminar courses were carried out under the aegis of Dr. David J. Vail, Medical Director to the Department of Public Welfare. He has now turned its operation over to the Minnesota State Medical Association, under the direction of Dr. Richard Magraw of the University of Minnesota Medical School.

The idea is beginning to catch on faster now, but not fast enough, because it is not adequately funded. Having had the privilege of being in private practice for many years and knowing what a high percentage of my patients had either frank psychiatric illnesses or psychosomatic disorders, I was able to appreciate the value of these seminar courses such as we had, and which are now being held in various sections of the State.

Over the years, and especially after attending these seminars, I learned to take care of many of the more seriously ill psychiatric patients, both before as well as after they had been under the care and guidance of private psychiatrists or had been returned to their communities from the several State Mental Hospitals.

Now that I have been in the St. Peter State Hospital working with these people for the past two years, I have been able to see more clearly than I did before the real urgency for you as physicians to become familiar once again with these problems. It is equally important for you to be willing to take care of these folks when they are returned to your care from private or public psychiatric hospitals. As far as I am concerned, it makes no difference whether you are a family physician or a specialist, all of you need to know better how to deal with these people when you see them. They comprise the bulk of your practice in one way or another, and too many of you tend to slough them off as "neurotics" instead of learning how to handle them as effectively as you can.

These folks come to you because they want you in preference to someone else, and you can do them a tremendous service by trying to care for them, difficult though many of them are. If you don't do it, and if they keep wandering from one doctor to another, they will eventually wind up being cared for by some "quack" or agency.

Continued to page 208.

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Carcinoma of the Pancreas and the Ampulla of Vater*

Treatment of

YOSHIO SAKO, M.D., Ph.D.**
Minneapolis, Minnesota

RADICAL PANCREATICODUODENECTOMY for carcinoma of the ampulla of Vater was introduced to surgeons of this era in 1935 by Whipple, Parsons, and Mullins.¹ Subsequently the two-stage operation was converted into a one-stage procedure, and in later years a number of minor changes were made, especially in the steps in reconstruction. In 1937 Brunschwig reported on the first radical pancreaticoduodenectomy for carcinoma of the pancreas.² There followed a wave of optimism for the operative procedure, but this was relatively short-lived among surgeons at large. As various clinics reported their experiences and the results were evaluated in the light of the operative mortality, the extent of prolongation of life and the relatively small number of five-year survivals, opinions have been voiced periodically that perhaps radical pancreaticoduodenectomy should be abandoned in favor of a less extensive palliative operative procedure. Recurrences have been reported as late as nine years after operation.³ Multicentric origin, of course, cannot be ruled out in such patients.

Despite the understandable lack of enthusiasm for the operation, abandonment of the procedure is not in keeping with progress. The operative mortality for pancreaticoduodenectomy is steadily falling and approaching 10% in a number of clinics. Abandoning of radical pancreaticoduodenectomy may deprive chances for cure to those who present with a picture of carcinoma of the head of the pancreas but who, in actuality, have an ampullary carcinoma which is well known to be potentially more curable than carcinoma of the head of the pancreas.

Incidence

Carcinoma of the pancreas accounts for 1

*Presented at the Minnesota Surgical Society Meeting, November 5, 1965.

From the Department of Surgery, University of Minnesota and Veterans Hospital, Minneapolis, Minnesota.

*See Test Your Word Score Page 221.

**Associate Chief, Surgical Service, Veterans Administrative Hospital.

to 2% of all carcinomas and is second in frequency to pancreatitis as a disease of the pancreas. Pancreatic carcinoma may occur in children and in young adults, but the majority of patients are in their fifth through seventh decade of life. Carcinoma of the pancreas occurs five times more frequently than ampullary carcinoma, and two thirds of the lesions occur in the head of the pancreas. The ductal type comprises 90 to 95% of the carcinomas and is the most malignant form. The tumor may also arise from the acini and the islet tissue.

Clinical Course and Pathology

The carcinoma may be only one half to one third of the actual tumor mass, usually the central portion, with pancreatitis accounting for the remaining areas. The tumor spreads relatively early to contiguous areas because of its retroperitoneal position and because the capsule is thin and there is no peritoneal coverage over much of the pancreas. The lymphatic drainage is rich and perineural spread occurs early. Its close relationship to and early involvement of many vital structures such as the portal vein, superior mesenteric artery and vena cava limit the resectability rate.

The usual clinical history of patients with carcinoma of the pancreas in its early stages contains very little to suggest the correct diagnosis. Physical, laboratory and x-ray findings cannot be depended upon at the beginning. The onset is insidious, and in many patients the symptoms are of a general nature common to a number of disorders such as biliary tract disease, peptic ulcer, and pancreatitis. By the time the so-called classical signs appear, 80 to 90% of the patients have passed the stage where complete surgical excision is possible; they will die of their disease in a few months.

Abdominal pain, jaundice, anorexia, and weight loss of insidious onset but becoming persistent are the major manifestations of carcinoma of the pancreas. Tumor compression of the pancreatic duct may produce pancreatic deficiency and result in changes in character of the stools. With involvement of the common duct there will be onset of

jaundice, and usually this is the single event which makes the patient seek medical aid.

Silent Growth

Carcinoma of the body and tail of the pancreas tends to grow silently for a longer period than in the head of the pancreas and then to cause severe pain as a predominant symptom. Jaundice occurs late and is usually a sign of wide extension of the tumor. The pain of carcinoma of the body of the pancreas is rather typical. Paroxysms of pain may begin near the umbilicus and radiate to the back. They may occur three to four hours after eating or may be totally unrelated to food intake. Relief is sought by the patient by sitting up and leaning forward or lying on the side with the legs drawn up. When these patients seek medical aid, the relative absence of positive physical findings and the occurrence of complaints out of proportion to the physical findings create a diagnostic problem. The generally distraught nature of these patients may on occasion be interpreted as a psychiatric disorder.

Progressive Jaundice

In carcinoma of the ampulla of Vater jaundice may be the first sign that all is not well. Initially the degree of jaundice may vary, but inevitably it becomes persistent and increasingly severe. Edema at the ampulla or slough of a portion of the tumor may cause intermittent obstruction. Jaundice tends to precede pain in ampullary carcinoma, but taken as a group, pain is the predominant early symptom of carcinoma of the pancreas and of the periampullary region.

When jaundice is present, hepatic function tests are useful in the differential diagnosis of obstructive jaundice. The serum bilirubin and alkaline phosphatase levels are high in extrahepatic biliary obstruction. Fecal urobilinogen output of less than 10 mgm. is diagnostic of high-grade biliary obstruction.

The relationship between diabetes and carcinoma of the pancreas is not clearly established, but when a patient in his sixties presents sudden onset of diabetes and particularly if the diabetes is difficult to manage

and there is weight loss and abdominal pain, carcinoma of the pancreas should be suspected. At times an abnormal glucose tolerance test may be an early clue.

Phlebitis

Migratory phlebitis has long been associated diagnostically with carcinoma of the pancreas. There appears to be no greater incidence of phlebitis in carcinoma of the head of the pancreas, but carcinoma of the body and tail of the pancreas is definitely associated with more than the expected incidence of phlebitis.⁴ An elevated blood trypsin level appears to be related to the accelerated blood coagulation. Thrombogenic substances have been observed in the blood of patients with other types of carcinoma such as carcinoma of the stomach, lung, and certain of the ovarian tumors; hence the increased incidence of phlebitis is not peculiar to carcinoma of the pancreas.

The findings on physical examination in patients with early carcinoma of the pancreas may be very scant. An abdominal mass is rarely palpable because of the relatively deep position of the pancreas. Usually, the gallbladder is readily palpable because of the distensible extrahepatic biliary system, in contrast to the gallbladders of patients with calculus obstruction (Courvoisier's law).

Laboratory Observations

The occurrence of blood in the stools is suggestive of duodenal erosion or ampullary carcinoma. Signs of pancreatic insufficiency are in general a late sign. Duodenal aspiration and examination for alteration in pancreatic function and the findings of abnormal cytology may strengthen or confirm the diagnosis of cancer, but most of these tests are not readily available to physicians at large and in most hospitals.

There are no early x-ray findings of pancreatic carcinoma, since direct visualization of the pancreas by radiographic means is not possible. The occurrence of changes due to pressure either externally or from encroachment on the surrounding structures is gen-

erally a late sign of the disease. Thus, widening of the duodenal loop or the pressure on the medial wall of the second portion of the duodenum (reverse three sign) is a relatively late manifestation. At times an ampullary carcinoma may be detected early by barium contrast studies of the duodenum. A distressing observation is that frequently patients with completely negative radiographic findings may be found at laparotomy to have a widely disseminated carcinoma.

Surgical Observations

Exploratory laparotomy may not readily solve the problem of diagnosis and treatment. Despite the freedom with which laparotomy permits one to inspect, palpate, and biopsy the questionable areas, the diagnosis may be in doubt and the surgeon be compelled to proceed on a presumptive diagnosis.

Biliary Structures

Carcinoma is most likely the underlying cause of biliary obstruction when there is a distended but thin-walled common duct and gallbladder. The duodenum and pancreas should be mobilized to permit palpation of the common duct and head of the pancreas. A systematic examination including multiple biopsies and frozen-section microscopic examinations is made to determine if the tumor has spread outside the pancreas. The lesser omental bursa is opened and biopsy taken of the lymph nodes surrounding the pancreas and in the area of the porta hepatis and root of the mesentery. Any tumor involvement in these areas precludes resection. The duodenum is mobilized (Kocher maneuver)* and the duodenum and pancreatic head reflected to the left to permit examination of the portal vein and superior mesenteric artery. Any involvement of the major vessels precludes resection. At times detection of vessel involvement may be found only after operation has progressed to the point where it must be continued, a situation to be avoided if possible.

The Duodenum

An ampullary carcinoma may be palpable as a mass through the duodenal wall; how-

*See Test Your Word Score Page 221.

ever, at times a small ampullary carcinoma will be detectable only upon opening the duodenum because, unlike pancreatic carcinomas, an early ampullary lesion tends to be soft and is difficult to detect through an intact bowel wall. On occasion it may be difficult to determine if the lesion is in the terminal common duct, ampulla, or the head of the pancreas. The common duct is explored to rule out impaction or erosion of stone into the intrapancreatic portion of the common duct. Here a cholangiogram may prove helpful.

Operative Procedures

Few take issue with the practice of taking a biopsy of an ampullary lesion; but when there is a mass in the pancreas, opinion is divided as to whether one should establish a positive tissue diagnosis before proceeding with pancreaticoduodenectomy or to proceed on the gross findings only.

Biopsy

Objections to biopsy of the lesion are that the carcinoma may be disseminated; that complications such as leakage of pancreatic juice may occur should resection not be done, and finally that multiple negative biopsies cannot be relied upon with absolute certainty that there is no carcinoma. Those who insist upon a positive biopsy contend that the magnitude of the operation of pancreaticoduodenal resection should not be undertaken without a tissue diagnosis. In general, those who have had the widest experience with pancreatic surgery tend to proceed on the gross findings only, but they recognize that there is a chance that pancreaticoduodenectomy may be performed for a benign lesion.

In Orr's review in 1952 he found five instances of pancreaticoduodenectomy for what proved to be a benign lesion.⁵ Three of these patients died as a result of the operation. At the Lahey Clinic, where biopsy was done infrequently, there were six instances of pancreaticoduodenal resection for a benign lesion among 216 operations.⁶ Carlson⁷ reported that the incidence of mistaken diagnosis of carcinoma ranged from 10 to 19%. The preferred method of biopsy is a trans-

duodenal needle biopsy, as it avoids leakage of pancreatic juice into the peritoneal cavity. The biopsy needle is directed at the central portion of the mass since the peripheral induration is usually due to pancreatitis.

Pancreaticoduodenectomy

The operative steps in pancreaticoduodenectomy are now quite well standardized. The one-stage operation is preferable and consists of subtotal pancreatectomy, total duodenectomy, removal of the gallbladder and distal one half or more of the common duct, hemigastrectomy and vagotomy. Reconstruction consists of a pancreaticojejunostomy, choledochojejunostomy, and gastrojejunostomy. Whenever possible, the pancreaticojejunostomy is made with a mucosa-to-mucosa suture of the pancreatic duct to the jejunal mucosa; but when this is not possible, implantation of the transected pancreas into the jejunum, as described by Waugh,⁸ is felt to give added protection against pancreatic juice leakage, a complication dreaded by all surgeons.

TABLE 1
Carcinoma of the Pancreas and Periapillary Area 1950-1964

Total patients explored (all males)	119 pts.
Age range	40-77 yrs.
Average age	61 yrs.
Average duration of symptoms	2.5 months
Pain	72 (60.1%)
Jaundice	86 (72%)
Weight loss	83 (70%)
Location of lesions	
Head	86
Ampulla	18
Body	18
Terminal common duct	1

TABLE 2
Operative Procedures

Laparotomy and biopsy only	32	21 patients deteriorated rapidly and were dead within 2 weeks. 60 patients recovered from the operation and survived a mean period of 3.2 months.
Palliative procedure	49	
Total	81	
Pancreaticoduodenectomy	38	Resection rate 32% — Details in Table 3.
Total	119	

Experience at the Minneapolis Veterans Hospital

The records of 119 patients, all male, operated upon during a 14-year period (1950-1964) for carcinoma of the pancreas and periampullary area were reviewed (Table 1). An accurate determination of the location of the tumor could not be made in all instances, but carcinoma was in the head of the pancreas in 86 patients, in the ampulla in 18, in the body of the pancreas in 18, and in the terminal common duct in one (Table 1). All the tumors were adenocarcinomas.

Palliative Procedures

The operative procedures are listed in Table 2. Laparotomy and biopsy only was done in 32 patients. These patients had extensive liver metastases, carcinomatosis or infiltration of the porta hepatis; hence even a palliative procedure appeared contraindicated. Palliative procedures in 49 patients consisted of cholecysto or choledochojejunostomy and gastrojejunostomy where obstruction appeared imminent. Twenty-one of these patients deteriorated rapidly and were dead within two weeks. Sixty patients recovered from the operation and survived a mean period of 3.2 months. The longest survivor lived 11 months.

Pancreaticoduodenectomy

Pancreaticoduodenectomy was done in 38

of the 119 patients. The procedures consisted of 25 resections for carcinoma of the head of the pancreas, 10 for carcinoma of the ampulla, two for lesions of the body and one for carcinoma of the distal common bile duct involving the duodenum and pancreas (Table 3). The average age of the patients with carcinoma of the head of the pancreas was 60 years. Sixteen had significant pain as a presenting complaint, 24 had jaundice, and 21 had weight loss ranging from 10 to 60 pounds. There were five postoperative deaths (20 per cent). The average postoperative survival was 12 months. Three of the longest survivals were as follows: one patient survived 41 months but died at the age of 58 with recurrence of cancer; the second patient is alive at 36 months at the age of 64 and in fairly good health except for emphysema, and the third patient is alive and well at 24 months. In the patient still alive at 36 months there was carcinoma in a lymph node adjacent to the pancreas and perineural invasion with carcinoma. Two patients in this group had total pancreatectomy. One patient, in addition to the total pancreatectomy, had a portocaval shunt because of vein involvement. He survived ten months and died of recurrence. Fifteen patients had carcinoma in the lymph nodes and seven had perineural invasion with carcinoma.

Ten patients had pancreaticoduodenec-

TABLE 3
Pancreaticoduodenectomy*

Location of Tumor	# of Cases	Operative Mortality	Average Survival	Longest Survivals
Head	25	5 (20%)	12 months	One survived 41 mo., died of recurrence; one alive at 36 mo., and one alive at 24 mo.
Ampulla	10	0	40 months	One each alive at 28 mo. and 7 yrs. One died 7 yrs. postoperatively at age 74 of cerebral vascular accident, and one 9 yrs. postoperatively at age 74 of coronary heart disease. Autopsy in both patients showed no recurrent tumor.
Body	2	1 (50%)	1 died at 6 wks. 1 died at 15 mo.	
Terminal common bile duct	1	0	17 months	
Total	38	6 (15%)		

*Total pancreatectomy was performed twice, one for a lesion in the head, one for an ampullary carcinoma. All others are subtotal resections.

tomy for carcinoma of the ampulla of Vater. There was no postoperative death. The average survival period was 40 months. At the time of this report one patient is alive at 28 months and one at seven years, both in good health. One patient died seven years postoperatively at the age of 74 because of cerebral vascular accident and another nine years postoperatively at age 74 of coronary heart disease. Autopsy showed no tumor in either patient. Another patient died two years after a previous ampullectomy followed by recurrence of carcinoma.

Carcinoma of the body of the pancreas was resected in two patients. One patient survived 15 months and died of recurrence. At the time of the operation there were metastases to the regional lymph nodes. The second patient, aged 45, had a portacaval shunt along with the pancreaticoduodenectomy. He expired six weeks postoperatively of peritonitis and renal shutdown. An au-

topsy showed multiple metastases to the liver.

Postoperative Complications

Postoperative complications after pancreaticoduodenectomy are listed in Table 4. Complications occurred in 10 of the 20 patients who survived pancreaticoduodenectomy for carcinoma of the head of the pancreas. There were three instances of severe postoperative bleeding, two of subphrenic abscesses requiring drainage, and three of infection of the abdominal wound requiring drainage. One patient had a wound hematoma requiring reoperation, and another, listed as having a subphrenic abscess, also required prolonged bile drainage.

Postoperative complications in the group in whom pancreaticoduodenectomy was done for ampullary carcinoma consisted of two instances of wound infection requiring drainage and one case of massive gastric hemorrhage 23 days postoperatively, which required conversion of a previous 40% stomach resection to 75% resection because of a gastrojejunal ulcer. This patient survived nine years and died at age 74 of coronary heart disease.

The causes for the six postoperative deaths were as follows: three patients had severe hemorrhage; one patient had bleeding, renal shutdown and peritonitis, and died 31 days postoperatively; another had bile leakage, peritonitis and uremia, and died on the thirteenth postoperative day, and the sixth patient died of peritonitis six weeks postoperatively (Table 5).

Discussion

In presenting our own experience, separation of carcinoma of the pancreas from carcinoma of the ampulla of Vater was made because the true picture of carcinoma of the pancreas cannot be presented when both types are grouped together. Preoperatively, however, it is of only academic interest to attempt to distinguish the origin of the lesion; similarly at operation it is not absolutely essential that one know the exact origin, since the operative maneuvers are basically identical. However, in evaluating

TABLE 4
Nonfatal Postoperative Complication

	Survivors	No. of Complications	Type
Ca head	20	10 (50%)	3 severe postoperative bleeding, 2 subphrenic abscesses, 3 infected abdominal wounds, 1 wound hematoma, 1 prolonged bile drainage
Ca ampulla	10	3 (33%)	2 wound infections, 1 hemorrhage from gastrojejunal ulcer treated by 75% gastrectomy
Ca body	1	0	
Ca terminal common duct	1	0	

TABLE 5
Causes of Postoperative Death

	No. of Patients	Postoperative Deaths	Cause of Death
Ca head	25	5 (20%)	3 severe hemorrhage 1 hemorrhage and uremia 1 bile leakage, peritonitis, uremia
Ca body	2	1 (50%)	Peritonitis

the results it is essential to separate the two types, because identifying them both as carcinoma of the pancreas presents a too favorable view of actual carcinoma of the pancreas and a relatively unfavorable picture of carcinoma of the ampulla.

Even the surgeon most experienced in pancreatic surgery cannot tell for certain the origin of the tumor of the head of the pancreas, the terminal common duct and the ampulla of Vater. In the absence of contraindications to pancreaticoduodenectomy, the operation should nevertheless be performed; because if, on the basis of a gloomy outlook for carcinoma of the pancreas, one were to do only a palliative procedure, he would deny the patient who has carcinoma of the ampulla of Vater an opportunity for cure. This point is emphasized by all who have extensive experience in pancreatic surgery.⁶

In our own experience, because of the large number of surgeons performing the operation, and generally most of these younger men on the staff, no one was able to accumulate any significant experience with pancreatic surgery. However, it is gratifying to find that the mortality rate was no higher than that reported by other groups. In evaluating the operative reports it was readily apparent that because of the surgeon's inexperience it was only rarely that he proceeded without a tissue diagnosis. Even if the tissue diagnosis had not been made, biopsy had been taken. The operability rate of 31% appears too high. Records show that in five patient after the operation was well under way, spread of carcinoma was found but pancreaticoduodenectomy was carried to completion.

Several of the recent reports are quite instructive in this respect. In 1958 Porter⁹ reported on the complete experience of treatment of carcinoma of the pancreas from Columbia University. There were 259 histologically proven diagnoses of carcinoma. It was found that in the cases of 38 patients who had had pancreatic resection, even the most experienced surgeon could not be trusted in his interpretation of the origin of the tumor. There was no five-year survival in

adenocarcinoma of the pancreas. Based on the surgeons' program of detailed examination of the nodes surrounding the pancreas and of the regions where early spread occurs it was found that the operability rate for carcinoma of the pancreas fell from 21.1% to only 6.8%. In contrast, the operability rate for carcinoma of the ampulla of Vater fell from 70% to 66.6%.

Glenn³ reported on a thirty-year experience from the New York Hospital and concluded that in his and his colleagues' hands carcinoma of the pancreas was an incurable disease. Of 25 patients who underwent radical pancreaticoduodenectomy four lived more than two years, one of these surviving nine years and then dying of recurrent carcinoma. Despite the poor results Glenn concluded that the procedure was worth continuing, because no patient survived a full two years following any procedure other than pancreaticoduodenectomy.

Other more recent results are reported by Monge, Judd and Gage from the Mayo Clinic,¹⁰ where eight patients survived five years after pancreaticoduodenectomy for ductal carcinoma, a five-year survival rate of 14.3%. Out of 46 patients 18 patients were still living five years after excision of carcinoma of the ampulla of Vater, a 39.1% five-year survival.

Conclusions

Surgical cure of pancreatic carcinoma is difficult to attain. By the time the so-called classical symptoms appear, 80 to 90% of the cases have passed the stage where complete excision is possible. Most reported series including our own have no five-year survival; however, 14% five-year survival attained by one group suggests that the operation should be continued in selected cases. All agree that longer survival occurs in the group treated by pancreaticoduodenectomy rather than by a palliative procedure, although one might argue that selection automatically occurs in such instances.

Carcinoma of the ampulla of Vater and of the pancreas behave differently. Five-year survivals of over 30% are reported by others, and similarly in our group, three of ten patients lived over five years. In two late

deaths (7 and 9 years postoperatively) autopsy revealed no recurrent tumor. These results alone justify continuation of radical pancreaticoduodenectomy for resectable le-

sions of the head of the pancreas since one cannot always separate with certainty lesions of the ampulla of Vater from some lesions of the head of the pancreas.

References

1. Whipple, A. O., Parsons, W. B., and Mullens, C. R.: Treatment of Carcinoma of the Ampulla of Vater. *Ann Surg* 102:763, 1935.
2. Brunschwig, A.: Resection of the Head of Pancreas and Duodenum of Carcinoma. *Surg Gynec Obstet* 65:681, 1937.
3. Glenn, F.: Carcinoma of the Pancreas. *Ann Surg* 159:945, 1964.
4. Sproul, E. E.: Carcinoma and Venous Thrombosis: The Frequency of Association of the Carcinoma in the Body or Tail of Pancreas with Multiple Venous Thrombosis. *Amer J Cancer* 34:566, 1938.

5-10 May be secured from the author or the reprints.

Medical Men and Music*

Eighteenth century William Withering (1741-1799) of Birmingham, pioneer in the use of digitalis for heart disease, played both the harpsichord and the flute, and Edward Jenner (1749-1823), pathological anatomist, performed on the flute and the violin.

For vocal music Sir Robert Christison (1797-1882) of Edinburgh, author of the first work on toxicology, distinguished himself.

"As a singer, both as a soloist and in part-songs, Sir Robert took a high place among the amateur musicians of Edinburgh. He was gifted with a bass voice of unusual power and good quality; and although he never had time to take lessons, constant practice in quartet singing and in small musical societies brought his voice to some degree of cultivation. . . . Sir Robert's voice retained much of its power and quality till he was past seventy, and he did not give up taking an occasional share in part-singing for several years afterwards. The last occasion on which he joined in anything of the kind was on the eighty-third anniversary of his birth, when he took the bass part of Bishop's well-known 'Mynheer Van Dunck'."**

In nineteenth century Germany Friedrich Henle (1809-1885), eminent histologist, performed so well on the violin, viola, and violoncello that he could join any extemporaneously arranged string quartet and acquit himself creditably. And Albert Billroth (1829-1894), noted surgeon, enjoyed music both passively through appreciation and actively through performance. In rhapsodizing on the rendition of "Manfred" he said:

"Manfred! Ah, but you should have heard and seen it! Reflections are useless, it is indescribable; full-blooded poetry and full-blooded music! It is stunning in a sensuous way; one dreams, one floats in the soft air without effort."**

Of his own keyboard facility he said:

"At this moment my fingers tremble after playing Bach for an hour. That is a tremendous tax for the fingers, for not only each measure, but the whole must be shaped forth like a Gothic stone structure, tall and great. This morning I have given myself up to this music with a kind of passion."**

* * *

After all, who more appropriate than medical men to carry the Olympic torch for the Greek doctrine of the unity of health and harmony!

*See *Minnesota Med* 49:1700, 1966.

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Management of Head Injuries

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THE FREQUENCY of head injuries from vehicular accidents justifies repeated emphasis of therapeutic principles underlying care of accident victims. The great majority of head injuries can and should be managed in community hospitals by nonspecialists in neurosurgery. However, recognition and initial care of those few cases which should be transported to a neurosurgeon is no less important. This paper emphasizes aspects of closed head injuries which we believe are basic to proper management.

The subject has been divided into four phases to present a systematic, step-wise approach to the head-injured patient. Associated injuries and management of the head injury will be described accordingly.

Emergency Treatment

Airway

An adequate airway must be secured and maintained before anything else is done. No injury takes precedence over the airway and no other measures should be undertaken until an airway has been established. This may require nothing more than positioning; but often, particularly in the seriously injured patient, tracheostomy is the wisest course. Tracheostomy is rarely done unnecessarily and is best done selectively. A head injury itself does not cause tachypnea, cyanosis or stertorous** breathing. Brief anoxia may produce irreversible cerebral damage in critical situations, and the airway must always receive first priority.

Control Bleeding

Active bleeding must be stopped, which generally means securing a lacerated major artery in the face, neck or extremities. The

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bleeding scalp can be temporarily controlled by firm pressure with the fingertips or by a firm dressing. Persistent bleeding from the scalp is managed by placing a hemostat on the galea and turning it over the scalp edge. In practice, scalp bleeding is seldom more than a troublesome ooze which can be stopped by a firmly applied, sterile dressing.

Treatment of Shock

The third immediate problem is shock, which should be treated without regard for the head injury. Cerebral concussion may be accompanied by a "shock-like" state, the duration of which is a matter of minutes. With this unimportant exception, head injury alone never produces shock. Although considerable blood can be lost from a torn superficial temporal or occipital artery, rarely is blood loss from the scalp sufficient to be shocking. The cause must be sought in the thorax, abdomen, pelvis or extremities. In the shocked patient, administration of blood or blood substitutes is the only method of restoring the cerebral circulation. The Trendelenburg position does not improve cerebral blood flow in the hypotensive patient, and venous congestion in the head-down position is deleterious.

Evaluation and Establishment of Baselines

The History

A good history is invaluable, and facts relating to the accident should be gleaned from any witness. The patient's state of health immediately prior to the injury as well as any past history of disease of the nervous system, alcoholism, or major medical illness should be learned, if at all possible.

The Physical Examination

The general physical examination should be thorough and systematic, and even in the unconscious patient general examination should precede the neurological examination.

Vital signs will approximate normal values in uncomplicated head injuries. A rapid rise in intracranial pressure produces bradycardia, a rise in systolic blood pressure, and slowing of respiration, in that order. A deviation of vital signs from the normal range

may be due to cerebral or, more commonly, to extracerebral causes.

Very early after injury, the course of a *fracture may be delineated* accurately by an overlying ridge of local edema. Crepitus beneath the scalp may be secondary either to air forced through a laceration or to fractures into a paranasal sinus. A "doughnut hematoma" of the scalp invariably feels like a depressed fracture; but regardless of the impression gained by palpation, the diagnosis of depressed fracture should not be made without radiographic confirmation. Fractures of the facial bones and jaw do not require immediate attention, unless threatening the airway, but their presence should be determined before facial edema precludes adequate examination. The orbits and zygomas should be palpated, the maxilla rocked by traction on the upper incisors, and the lower jaw checked for dental occlusion, mobility, and crepitus. If facial edema is already present, assume the presence of facial fractures.

The ears should be examined for the presence of blood within the external canal or behind the tympanic membrane, as the finding of blood in either site indicates a *basilar skull fracture*. Ecchymosis over the mastoid tip is equally significant.

Epistaxis, in the absence of significant direct trauma to the nose, and cerebrospinal rhinorrhea indicate a basilar fracture into one of the paranasal sinuses. The treatment of basilar fractures will be considered later. Damage to the eyeball or its adnexa should be determined before periorbital edema closes the eyelids.

Local tenderness or a *displaced spinous process* may indicate a fracture of the cervical spine. A patient in coma does not resist movement of the neck, and a supple neck in the unconscious patient does not exclude a spinal injury. Evidence of trauma to the anterior cervical region should alert the examiner to the possibility of injury to the trachea and carotid artery. Direct trauma to the carotid artery can induce arterial thrombosis with infarction of the cerebral hemisphere and hemiplegia which may be

attributed mistakenly to an expanding intracranial hematoma.

Abdominal paracentesis is an invaluable diagnostic procedure and is mandatory when the cause for shock cannot be explained by other extracranial injury. Ruptured spleens appear to be notoriously common in patients with head injuries. Head injuries do not cause ileus; but thoracolumbar fractures, with or without spinal cord injury, are regularly followed by reflex paralytic ileus.

As part of the general examination, a *nasogastric tube* is passed for evacuation of the stomach contents, which makes vomiting less likely and circumvents aspiration of vomitus. Swallowed blood is usually found with extensive facial injuries and will be vomited if not removed. The nasogastric tube may be left in place and attached to low suction. An indwelling urethral catheter should be passed in all unconscious patients and in those unable to void voluntarily. Examination of the urine for blood should be carried out immediately to exclude injury to the urinary tract.

Neurologic Examination

The level of consciousness is determined by graded stimuli. Starting with commands spoken in a normal tone, stimuli of increas-

ing intensity are applied to the point of responsiveness. With minor variations, the stimulus and response will remain constant or indicate a return toward a fully conscious state during the early period of observation. The stimulus may be anything from calling the patient's name in a normal tone to firm supraorbital pressure. The response may be an opening of the eyes or purposeless shifting of position and withdrawal from pain produced by the examiner.

The state of consciousness is the most important observation, and it must be recorded for future reference. The following terms describe the level of consciousness: *coma*: unresponsive to all stimuli; *areflexic** except for a direct tracheal cough reflex; *semi-coma*: responsive to noxious stimuli; response may be purposeful, but unable to carry out commands; *stuporous*: confused, faulty recognition; may carry out simple command after coaxing; *sleepy*: easily aroused.

The pupils are checked for equality and reaction to light. Minor inequalities may come and go and, if transient, are unimportant. Direct blows to the eye produce traumatic mydriasis which may persist for hours or days. Sympathetic involvement is uncommon, but a Horner's syndrome may account for pupillary inequality. With these exceptions, *unilateral dilatation of a pupil* pre-

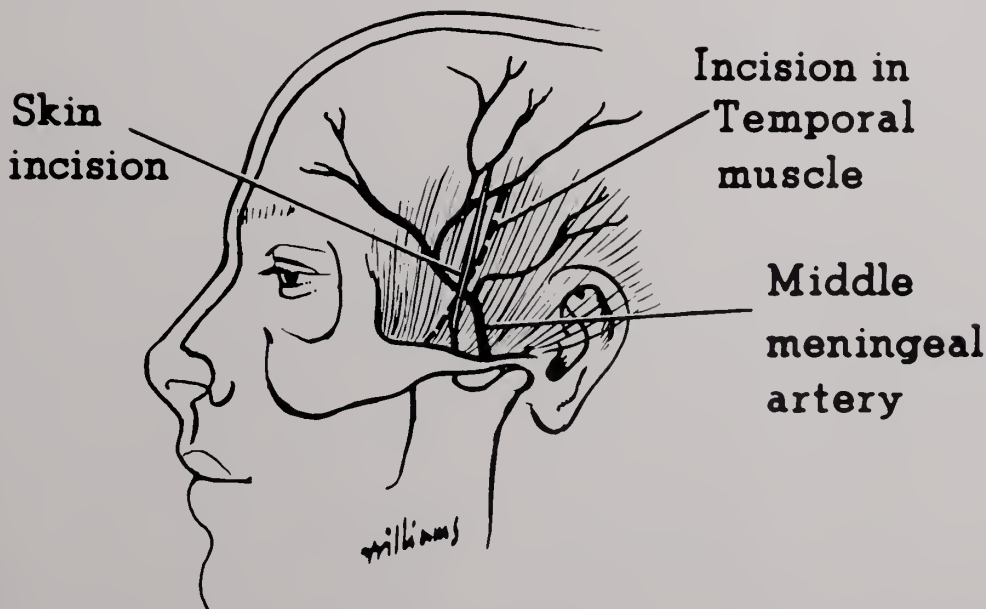


Figure 1

**See Test Your Word Score Page 221.

sumes a mass intracranial lesion requiring surgical intervention. Bilateral dilated and fixed pupils indicate a hopeless situation; we know of no patient with a neurosurgical condition who has ever recovered after manifesting this ominous sign. Do not use mydriatics; the information gained by funduscopic examination does not warrant loss of the important pupillary reaction.

Cerebral hemisphere function can be assessed by observing spontaneous or induced movements of the extremities. Hemiparesis evident immediately following injury is most often due to cerebral contusion, whereas hemiparesis appearing later is assumed to be caused by an intracranial hematoma. Speech must be evaluated in keeping with the patient's conscious state. A minor aphasic disturbance may be a valuable initial observation.

Reflex activity has the advantage of objectivity and the usual reflexes should be tested. Bilateral Babinski responses are not uncommon in patients with head injury or subarachnoid hemorrhage, and in the post-seizure state. The early presence of decerebrate or decorticate rigidity indicates initial injury to the brain stem. The late appearance of these responses is due to herniation of the brain with secondary brain stem compression and indicates a dynamic process requiring investigation.

Damage to the *optic or oculomotor nerves* can be determined by direct and consensual pupillary reactions to light. The extra-ocular muscles are not examined individually, but the range and nature of spontaneous and induced eye movements should be recorded. Eye movements are best elicited by rapidly turning the head, first to one side and then to the other. Disconjugate eye movements indicate either deep coma or primary injury to the brainstem with involvement of the pathways connecting the nuclei of III and VI. The facial nerve is easily tested. Peripheral facial palsy occurs with basilar fractures into the ear and may be immediate or delayed in appearance. In the presence of facial weakness, the cornea may require protection by temporary closure of the eyelids with a strip of adhesive which can be re-

moved periodically for inspection of the pupil.

Roentgenograms

Skull roentgenograms should be taken only after emergency treatment. The value of early examination is limited, but certain findings may be of great importance. Properly positioned films permit recognition of pineal shift, fracture into an air-containing paranasal sinus, fracture across the middle meningeal groove or a major venous sinus, the presence and extent of depressed fractures, and compound fractures not suspected by physical examination.

Every unconscious patient should have anteroposterior and lateral views of the cervical spine. Otherwise, cervical fractures may go undetected and the patient may suffer additional damage to the spinal cord before recognition and proper treatment of the spinal injury.

Lumbar Puncture

We do not utilize lumbar puncture in the management of acute head injuries. Lumbar puncture should be performed if meningitis is suspected, a situation which may arise several days after the injury. In addition it may be of some value in the comatose patient with no history, in whom a head injury must be excluded.

Management of Head Injury

Provided that there is historical, external, or x-ray evidence of injury to the head, a patient should be managed as a head-injury case. This statement applies particularly to alcoholics, epileptics, and "strokes."

A trivial head injury can become a fatal head injury. Every hour, more or less frequently, depending upon the patient's condition, the following observations should be made and recorded on a separate sheet with orders to notify the physician if:

(1) Pupils originally equal become unequal. (This may be impractical in understaffed areas.)

(2) The neurologic status deteriorates. (By deterioration is meant the development of new neurologic signs, a depression of the

state of consciousness, or unilateral pupillary dilatation.)

(3) Pulse rate becomes less than 60 or greater than 130.

(4) Respiratory rate becomes less than 16 or greater than 34 (or irregular).

(5) Systolic blood pressure becomes less than 100 or greater than 150 (in the young adult).

Observation is understandable when one considers the purpose and limitations of neurosurgical intervention. An operation can relieve increased pressure and terminate compression of contiguous structures produced by a hematoma. Fortunately, most hematomas develop slowly and announce themselves by producing gradual deterioration in a patient's condition; therefore, if a baseline is established soon after the injury, failure to improve or regression from the baseline status can be recognized. On the basis of serial observations, any deterioration in a patient's neurologic status is an indication for excluding an expanding hematoma as the cause.

Care of the Unconscious Patient

Aspiration of vomitus is often fatal and vomiting may be delayed until the second or third day, especially when blood is present in the stomach. Good practice in the unconscious patient is insertion of a nasogastric tube attached to suction. The patient should be turned side to side every hour. The flat supine position is best for examination, but should not be maintained because of the risk of aspiration. In the absence of pulmonary complications and shock, the head is best kept elevated 20-30 degrees to encourage venous return from the head.

The cornea should be protected from drying or abrasion. A strip of scotch tape over the lid is adequate. Hyperpyrexia must be treated promptly because it exhausts the patient's reserves and adversely affects the damaged brain. A temperature of 101° or above should be treated vigorously, and specific directions should be written for measures to reduce it. Hyperpyrexia, often delayed in onset for 12 to 36 hours, is best controlled by aspirin and sponging. Tube

feedings may be started at the end of 48 hours if the patient has had a tracheostomy, has not vomited, and if gastric fluid recovered by continuous suction is not excessive.

Intravenous fluids should allow a daily urinary output of about 1,000 cc. A small number of severely injured patients will retain or lose salt because of hypothalamic damage. Blood chemistries should be determined at least every other day for one week. Deliberate dehydration does not reduce cerebral edema and has no place in the management of acute head trauma. An indwelling urinary catheter lessens the nursing problem and permits accurate determination of urinary output in the unconscious or uncooperative patient.

Special Problems

Convulsive seizures may occur in patients with head injuries soon after injury. Many early seizures are focal, and characteristics of the seizure often indicate the site of cerebral irritation. Because a single seizure may progress into status epilepticus, convulsions must be treated vigorously. An early seizure does not indicate the presence of an intracranial hematoma. Seizures are best managed with phenobarbital, paraldehyde and dilantin, I.V. or I.M., depending upon the urgency of the situation. Sodium amytal and pentobarbital are not anticonvulsant drugs and should not be used for this purpose. Barbiturates are used with caution because of their respiratory depressant effect. An unobserved seizure may produce a confusing situation. Seizures produce hypoxia, adversely affect the head-injured patient, and must be controlled promptly.

The incidence of *traumatic diabetes insipidus* is low. Polyuria may appear early or late, usually several days after the accident, and characteristically commences with great suddenness. The use of aqueous pitressin simplifies fluid replacement. Headache may become a complaint with return of consciousness. The usual headache is similar to that which sometimes follows lumbar puncture. Persistent severe headache is unusual and warrants spinal tap if continued into the second week post injury. Subarachnoid

hemorrhage also produces headache which generally subsides in three to four days. The value of repeated spinal taps for relief of headache is questionable.

Restlessness to an extreme degree during the acute stage is uncommon, and if present its cause should be sought in a full bladder, an unrecognized fracture, extreme meningismus from subarachnoid hemorrhage, delirium tremens, or frontal lobe injury. Wrist and ankle restraints often aggravate the situation and should be used only as a last resort. Side rails and an attendant are preferable to any mechanical restraint. Sedation during the acute phase of injury depresses respiration and the level of consciousness, and is contraindicated, even in minor head injuries.

Basilar skull fractures into the middle ear or paranasal air sinuses often accompany severe head injuries, although they may follow relatively minor trauma. Fractures involving the ear are readily detected by otoscopic examination if the tympanic membrane is intact, or by the observation of blood or cerebrospinal fluid draining from the ear. Fractures into the frontal and ethmoid sinuses should be suspected in all patients with facial injuries. The diagnosis is established by observing cerebrospinal fluid rhinorrhea, remembering that in the supine unconscious patient this may go undetected. Fractures into the frontal and ethmoid sinuses are usually visible on roentgenograms. All basilar skull fractures are compound fractures by virtue of communication through a torn mucous membrane into an air-containing cavity. Treatment of basilar skull fractures requires therapeutic antibiotic coverage for at least seven days, and longer if leakage of cerebrospinal fluid persists. The conscious patient with cerebrospinal fluid rhinorrhea should be cautioned against nose-blowing.

Carotid-cavernous sinus fistulas may appear immediately, or as late as several weeks after injury. The fistula results from a tear in the carotid artery as it passes through the cavernous sinus and is characterized by pulsating exophthalmos and a cranial and orbital bruit. The condition does not require

emergency treatment, although most fistulas persist without surgical intervention.

Indications for Surgery

Compound Fracture

Open head wounds are injuries in which the intracranial contents are in open communication with the air through either scalp or skin. These are compound fractures, and treatment involves debridement and closure of the wound. Experience in World War II taught that patients with open wounds, unless fatally injured, do not deteriorate rapidly. They tolerate transfer by ambulance or by air to a hospital equipped for major cranial surgery. Compound wounds should be carefully debrided with water-tight reapproximation of the dura and accurate closure of the scalp without drainage.

Extensive compound wounds should be transferred to a neurosurgical center. Emergency treatment of the cranial wound should be limited to the application of a sterile dressing over the wound. Rarely will active bleeding from the scalp or exposed cerebral vessels constitute a problem. No attempt should be made to remove clotted blood or exposed brain which will only activate bleeding and introduce further contamination. The initial surgery should be definitive; nothing beyond the application of sterile dressing is indicated prior to transfer. Other emergency measures directed at establishing an airway, splinting long-bone fractures, and combating shock should be implemented when the patient is initially treated. Definitive debridement can be delayed up to 24-48 hours without a significantly increased risk of infection, provided prophylactic antibiotic therapy is started promptly.

Depressed Fractures

Depressed skull fractures with an intact scalp are treated as closed head injuries. The underlying brain is damaged at the moment of impact, and the continued presence of the depressed bone is not detrimental if the degree of depression is slight. Almost all depressed fractures should be corrected surgically, but rarely do they constitute an emergency.

Intracranial Hematomas

Subarachnoid hemorrhage, common even in trivial head injuries, produces meningeal irritation but requires no treatment and will not be discussed. Blood in significant quantity can collect on each side of the dura mater or within the brain. The former, extradural and subdural hematomas, lie on the brain surface and are accessible through trephine openings in the skull. The latter, intracerebral hematomas, are uncommon in the absence of depressed skull fractures, and the diagnosis is difficult to establish without special studies. Surface hematomas can be diagnosed and treated through burr holes. The remainder of the discussion will be confined to subdural and extradural hematomas.

Extradural Hemorrhage

Extradural hemorrhage is the one true neurosurgical emergency. A typical case will have minor trauma to one temple followed by a lucid interval of one to six hours, and then manifest signs of rapidly progressive compression of one cerebral hemisphere. A fracture crossing the middle meningeal groove is nearly always present. After an initial complaint of headache, weakness of one side of the body quickly appears with somnolence deepening to stupor and dilatation of the pupil on the side of the hematoma. The evolution of extra-dural hematomas is rapid because blood under arterial pressure is forced into the extradural compartment from a torn middle meningeal artery. Compression of the brain must be relieved immediately. Time does not permit transfer of the patient to another hospital and the blood clot must be evacuated without delay. Such a patient is probably the only one whose life will be saved by surgery performed in the first few hours after injury. The objective of surgery is an opening in the skull which will allow extrusion of the clot. The hematoma usually underlies the temporal fracture, and the first burr hole should be made at the fracture site. After enlarging the burr hole with rongeurs, the torn meningeal artery can be coagulated, clipped, or transfixed with sutures. If these measures fail, the bleeding will be considerably dimin-

ished by ligation of the external carotid artery in the neck. The surgeon on the spot must operate then and there, once the diagnosis is suggested. A neurosurgeon may be summoned by phone, but evacuation of the hematoma should not be delayed until he arrives. (See appendix for operative technique.)

Subdural Hemorrhage

Subdural hemorrhage can also be acute, with rapid deterioration necessitating surgery within the first 48 hours after injury. The bleeding is arterial but is caused by laceration of the brain with tearing of cerebral arteries. Brain damage is characteristically severe and blood in the subdural space is coincidental. The lacerated and contused brain swells rapidly, and evacuation of the small subdural hematoma accomplishes little or nothing. Mortality with acute subdural hematomas exceeds 90%. Rarely, acute subdural hematomas may develop from a torn venous sinus or Sylvian vein without significant damage to the brain. This latter hematoma mimics an epidural hematoma and is treated by the same principles.

Chronic subdural hematomas manifest themselves three to 12 weeks after injury. Minor and often forgotten trauma tears a vein bridging from the cortex to the superior sagittal sinus, and resultant venous bleeding is slow. Encapsulation and secondary enlargement produce the delayed onset of signs and symptoms. Drainage through exploratory burr holes is curative if brainstem compression has not reached the state of irreversibility.

Subacute subdural hematomas are intermediate between acute and chronic hematomas. Headache, progressive somnolence, and a generally unfavorable course prompt investigation at some time beyond the third day post injury. The outlook is favorable for satisfactory recovery.

Subdural Hygroma

Sometimes, particularly with a subacute evolution, one encounters a subdural hygroma rather than a hematoma. A hygroma consists of xanthochromic cerebrospinal fluid

probably resulting from a tear in the arachnoid. Clinically, hygromas cannot be differentiated from hematomas and they respond to drainage through burr holes.

Carotid angiography is being employed with increasing frequency as an accurate investigative study. Bilateral carotid angiograms permit localization of hematomas as well as demonstration of unsuspected pathology, but carotid angiography is a procedure for the expert because interpretation may be difficult.

The use of corticosteroids, hypothermia and hypertonic urea to decrease cerebral edema may have a place in the treatment of closed head injuries. Hypothermia requires equipment and nursing care available only in certain centers. Urea should not be used without excluding a mass lesion by burr holes or angiography; even then, its value is quite limited.

Emergency Surgery

Release Hematoma

Any hospital with facilities for major surgery should be equipped to perform burr holes for an epidural hematoma. In addition to the standard surgical instruments the following instruments should be available:

Hudson brace
McKenzie perforator
Cushing burr
periosteal elevator
mastoid retractor or self-retaining tissue retractor
angular double-action rongeur
Frazier suction tip
bone wax
(a Bovie unit is helpful but not essential)

Surgical Procedure

The skin incision is vertically placed 1½ inches behind the orbital process of the frontal bone, extending from the superior extent of the temporalis muscle to the zygomatic arch (Figure 1).

The temporalis muscle is stripped bilaterally from its attachment to the temporal bone and the muscle retracted with a self-retaining retractor.

A burr hole made in the thin temporal bone directly above the zygomatic arch is enlarged with a rongeur to expose the middle meningeal artery and the hematoma. The hematoma can be evacuated using forceps and the suction tip. Bleeding is controlled with electrocautery, ligatures and bone wax; diffuse oozing from dura can be controlled with fibrin foam and gentle pressure. If bleeding cannot be stopped, the wound can be packed and the patient transferred to a neurosurgical center.

If no hematoma is present at the first site, a second opening should be made over any existing fracture line.

Summary

The provision of an adequate airway, recognition and treatment of associated injuries, and maintenance of physiologic function in an unconscious patient constitute the basic management of closed head injuries. Regression from initial baselines indicates a dynamic process which warrants investigation to exclude or establish the existence of a treatable lesion.

Eyes are compacted powers; they are an index of vision; they see and refer us to greater seeing. Nor has the stomach a less noble office. It digests food; that is, in its own particular method, it deals with the nourishment offered by the universe. It is the physical formula of that health which destroys certain elements — the bacteria which harmfully approach us. By it we learn to consume; by it therefore to be, in turn, consumed. So even with those poor despised things, the buttocks. There is no seated figure, no image of any seated figure, which does not rely on them for its strength and balance. They are at the bottom of the sober dignity of judges; the grace of a throned woman; the hierarchical session of the Pope himself reposes on them. — Charles Williams

Percutaneous Non-Catheter Retrograde Brachial Arteriography*

Use
of the
Amplatz
Needle

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 BSTRUCTIVE VASCULAR lesions in the brachiocephalic arterial network may produce incapacitating symptoms in the patient who has cerebral-vascular insufficiency. Satisfactory surgical correction and re-establishment of arterial flow is possible for many of the extracranial vascular obstructions. Precise delineation of the extracranial and intracerebral arteries is a necessity for such surgical procedures. The diagnostic procedure should not increase the risk to these ill patients.

Percutaneous non-catheter retrograde brachial arteriography is a safe and reliable method to visualize three of the four major arteries and their branches in the neck and brain.^{1,2} By retrograde injection of the right brachial artery the contrast material will fill the right subclavian, the right vertebral, and the right carotid arterial systems. This includes excellent visualization of the basilar artery, the carotid siphon, and the major cerebral branches. Not only is the bifurcation of the right carotid artery well documented, but in 15% of the patients the cervical portion of the left carotid artery will be visualized, as the innominate artery gives common origin to both carotid vessels. Injection of the left brachial artery fills the left vertebral artery, the basilar artery, and its branches. The degree of visualization of these vessels is dependent upon variations in the natural anatomy, the disease processes, and the amount and rapidity of injection of the radiopaque medium.

In their descriptions other authors have reported the use of a thin-wall 17-gauge steel indwelling brachial needle through which the injection is made. A slight variation of

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the described techniques has been utilized at our laboratory. We believe that the use of an Amplatz teflon catheter-needle is less likely to produce complications with high pressure injection of contrast material and increases the safety of the procedure.³

The Amplatz catheter-needle consists of an outer flexible teflon sheath, a middle blunt steel needle, and an inner ultra-sharp pointed metal obturator (Figure 1). The teflon catheter has a standard Luer-lock fitting for secure attachment to the pressure injector connections.

Technique

Our experience with this technique has demonstrated its low risk even in the acutely ill patient. Because of this result, we would like to describe in more detail certain facets of the procedure which have proven helpful to the patient and to us so that consistent optimum x-ray visualization of the vessels is secured.

Preoperative Preparation

On the day prior to the event the surgeon

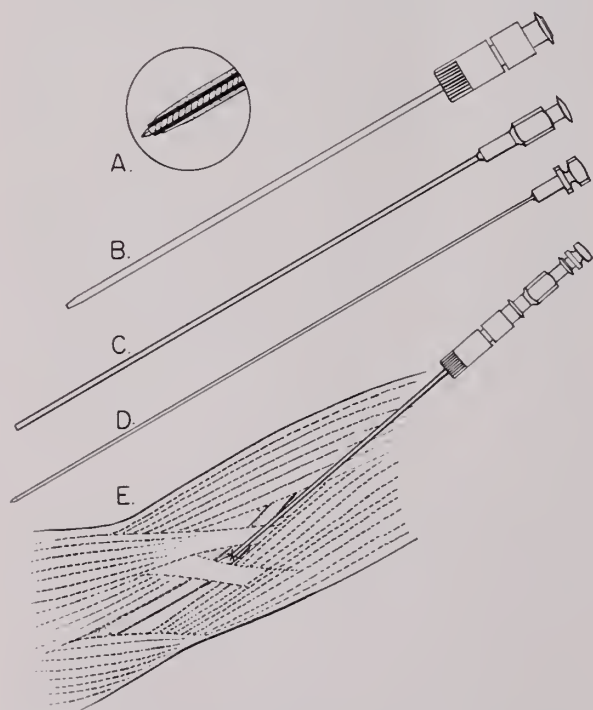


Fig. 1—The Amplatz needle and its component parts. A. Stylus tip of the assembled needle unit. B. Tapered teflon catheter and connector. C. Blunt hollow inner metal cannula. D. Solid inner stylus. E. Position of introduction into the brachial artery medial to the biceps tendon.

explains the salient points to the patient so that he has a clear understanding. (Obviously, this is not possible in certain individuals, as illness precludes understanding.) Preoperatively the patient receives an anti-histamine three hours before, a barbiturate two hours before, and an analgesic and atropine one hour before the injection. He is then placed on the X-ray table next to the bi-plane rapid film-changer unit. Scout x-ray films for proper position and technique are processed.

Introducing the Needle

During this interval the patient's arm is abducted and extended, a blood-pressure cuff placed on the forearm, and the antecubital and elbow area prepared and isolated with sterile drapes. The brachial artery is palpated. The skin puncture site, the V of the muscle junction in the forearm (Figure 2), is infiltrated with a local anesthetic as is the area of the artery. The skin is first "stabbed" with a No. 15 scalpel blade and an 18 or 19 Amplatz needle introduced through the stab wound and guided into and usually through the brachial artery.

The obturator is removed and the steel-teflon unit slowly withdrawn, slightly depressing the shaft. Entrance into the arterial lumen is signaled by a sudden pulsatile flow of blood and often a definite palpable "click." The teflon sleeve is advanced gently into the vessel lumen as the inner cannula is removed. Occasionally the teflon sleeve cannot be advanced without the aid of a coiled wire guide.

The Injection

Retrograde injection of contrast medium is made only if there is good pulsatile blood flow through the needle. The teflon catheter is connected to a CO₂ pressurized injector-syringe for rapid instillation of 40-50 ml. of 60% methylgluamine diatrizoate. The blood pressure cuff about the forearm is elevated to 200 mm. Hg. just before and decompressed immediately after the injection. A special person is assigned to this cuff inflation-decompression to avoid inadvertent maintenance of inflation and ischemic damage to the hand. The teflon catheter is disconnected from the injector and patency main-

tained by saline flushing during the processing of the X-ray films.

Only when satisfactory visualization of the vessels has been obtained does the operator remove the intra-arterial catheter. It has not been uncommon to make several injections with extreme postural changes of the patient's head in order to adequately see certain anatomical areas, especially the ver-

tebral artery origin. The right brachial artery is usually injected first and the left brachial artery, second.

Safety Measures

1. All patients are seen in consultation with a neurologist. Angiograms are not done if there is not unanimous agreement.

2. The radiologist determines the type and



Fig. 2 — Obstruction of origin of right vertebral artery. No filling of the right carotid artery occurs when this patient rotated his head to the right in the right posterior oblique position.



Fig. 3 — Obstruction of the internal carotid artery at the bifurcation. The vertebral artery is tortuous but non-obstructed.

amount of contrast media and injection pressure. Consultative pre-procedure discussion defines the pertinent vessels to be studied.*

3. The total amount of contrast media injected at one sitting is limited to prevent secondary brain injury; only in rare circumstance will this amount be exceeded. We feel that the patient should be returned for further studies on another day.

4. If the extracranial vessels are "normal," intracerebral arterial studies are usually recommended.

5. The left carotid system is visualized by direct percutaneous puncture or retrograde aortic arch injection.

6. Papaverine 15-30 mgm. is injected prior to removal of the needle.

*The authors are grateful to Drs. S. Feinberg and M. Goldberg for their valuable help.

Results

This technique has been utilized in 55 studies. Examples are demonstrated (Figure 3). There has been no adverse effect in any patient. There has been no nerve injury or ischemic sequela in any extremity. One patient had an absent radial pulse post study. In a few patients the procedure was terminated because of inability to satisfactorily cannulate the brachial artery. These patients were subsequently studied by other techniques and the x-rays were considered adequate but not optimum as compared to the retrograde non-catheter brachial arterial visualization. The Amplatz teflon-needle has proven a versatile, dependable instrument of considerable value and safety to this procedure.

References

1. Marshall, T. R., Ling, J. T.: Direct Percutaneous Noncatheter Left and Right Brachial Angiography — Right Cerebral Angiography. *Radiology* 80:258, 1963.
2. Marshall, T. R., Ling, J. T., Gonzales, R.: Additional Experience with Direct Percutaneous Noncatheter Brachial Angiography. *Radiology* 81:568, 1963.
3. Amplatz, K.: Percutaneous Arterial Catheterization and Its Application. *Amer J Roentgenol* 87:265, 1962.

PAROTITIS-HERPANGINA-COXSACKIE VIRUS SYNDROME

The coincident presence of proved Coxsackie virus, herpangina, and parotitis is rare. Four such cases have been reported by Howlett and associates. The infection is seasonal, occurring primarily in the summer months.

Aside from the parotitis the symptoms are similar to those of herpangina and consist of sudden onset of headache, sore throat, dysphagia, abdominal pain, and pyrexia, which continue for two or three days. The local vesicular or ulcerative lesions are usually limited to the tongue, anterior pillars, and soft palate. Involvement of one or both parotid glands occurs simultaneously. The Coxsackie group A virus, considered to be the cause of herpangina, was isolated from the tiny, 0.5-mm. greyish-white papulovesicular lesions of the oral mucous membrane as well as from the saliva of each of the four patients with parotitis. Spontaneous recovery is the rule, the mucous membrane lesions resolving within four to six days. No specific therapy is indicated.

Durham, Robert H. — *Encyclopedia of Medical Syndrome*
Hoeber Medical Division, Harper and Row, New York

Only Human

When you have to keep your back to the wall and your ear to the ground . . . your shoulder to the wheel and your nose to the grindstone . . . your head level and both feet on the ground — you're not a contortionist; you're just like the rest of us. — Phoenix Flame

|| Addiction

Cases Treated on a Psychiatric Service

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REVIEW OF THE problem of addiction in a general hospital psychiatric ward has become important because of the increasing use of new tranquilizing agents and non-barbiturate sedatives. This investigation focused on our experience with patients having the diagnosis of addiction on the Psychiatric Service of the University of Minnesota Hospitals.

Review of the Literature

Statistics regarding the incidence of addiction in the general population are unreliable and difficult to obtain. Rathod¹ emphasized that addictive people do not volunteer their problems and are diagnosed properly only when the physician is alert to the possibility of addiction. Schremly and Solomon² found that even with incentives to look for drug addiction, physicians failed to recognize a large number of drug abusers admitted to a general hospital and pointed out that of the known cases of addiction, only a small number of them were actually reported to official data-collecting agencies.

Blane et al.³ found that improper diagnosis in alcoholic patients is related to two factors: (a) a better social adjustment by the patient leads to missing or at least not diagnosing and treating the patient as an alcoholic, and (b) alcoholic patients with medical or surgical complaints tend to be missed as far as their addiction problem is concerned. They concluded that physicians prefer a medical diagnosis over a social or psychological diagnosis.

Since the introduction of the newer non-barbiturate sedatives and tranquilizers, records consist mainly of case reports and the incidence of their abuse cannot be ascertained. Meprobamate, glutethimide, ethina-

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mate, ethchlorvynol, methypylon, and chlordiazepoxide are several of the drugs known to have addictive properties.^{4,5} Physiological withdrawal symptoms similar to those of barbiturate withdrawal are described for these drugs.^{4,6}

The abuse of these drugs is real and serious beyond doubt, and deaths are known to have occurred following the withdrawal of barbiturates,⁷ meprobamate,⁸ and methypylon.⁹ Gradual withdrawal of the addicting drug is recommended to avoid complications in therapy. Grand-mal convulsions, hyperpyrexia, and delirium are regarded as symptoms of impending disaster.¹⁰ There is no general agreement about specific therapy to control seizures. Blachly¹¹ and Essig⁴ believe that diphenylhydantoin is ineffective in the prevention of seizures due to drug withdrawal, has a small but definable hazard in itself and is, therefore, contraindicated. Pearson and Little,¹² however, recommend using anticonvulsants in withdrawal addicting drugs while Wilhoit¹³ regards the use of diphenylhydantoin as essential in the treatment of alcohol withdrawal.

Method

This study was done in retrospect and thereby avoided influencing the ongoing practice in the hospital. Records were not examined until they were complete and filed in the record room. In order to find all the addiction cases, a double search of all records of patients admitted and discharged from the University of Minnesota Hospitals Psychiatry Service from January 1, 1963, to May 31, 1965, was made. The searches were made by (1) the use of an IBM registry and (2) a review of discharge diagnoses kept on file in the psychiatric office. In addition, a special search was made of all records where the problem of addiction might be related, such as in the cases of acute and chronic brain syndromes.

Findings

Incidence

During the time of the study there were 1,116 admissions to the psychiatric service. Addiction was found in 84 patients (7.5 percent of the total number of admissions). Of

TABLE I

Demographic Data			
Age	Number	Sex and Race	Number
20-29	14	White males	44
30-50	53	Indian males	1
51-68	17	White females	37
		Indian females	2
Marital Status	Number	Hollingshead Two Factor Index of Social Position	Number
Never married	18	Class I	22
Married once	42	Class II	5
Multiple marriages	10	Class III	9
Divorced or separated	13	Class IV	17
Widowed	1	Class V	29
Financial Status	Number	Unknown	2
County welfare	38	Final Disposition	Number
Private or partial private	41	Transferred to other institution	6
Special classifications	5	Continued outpatient psychiatry	23
Number of Admissions to This Hospital	Number	Family physician	16
1st admissions	58	Alcoholics Anonymous	14
2nd admissions	15	To self and family	13
3 or more admissions	11	Court and correctional	6
Previous Treatment	Number	Clergy	2
First Treatment	20	Medical or surgical	2
		Other	2

these, 44 patients had a diagnosis of drug addiction and 40 had a diagnosis of alcoholism. Fourteen of those patients who carried a diagnosis of addiction to drugs were known to use alcohol to excess and nine who received a diagnosis of alcoholism were also known to be abusers of drugs. In other words, 27 percent of the patients with addiction diagnoses were using both drugs and alcohol.

Demographic data* on our patients is summarized in Table 1. Forty-six came from communities over 2,500 population and 21 grew up in communities under 2,500 population. In 17 patients, the place of origin was absent from the records.

Forty-one patients (49 percent) were able to pay for all or part of their care in the hospital. According to the Hollingshead Two Factor Index of Social Position,¹⁴ 27 patients were classified in Class I or II. Sixty-four of the patients received previous treatment for addiction, while only 20 were being treated for addiction for the first time. Sixty-eight of the patients admitted to the hospital came on a voluntary basis, nine required a legal hold order, while seven were admitted in an emergency situation because of an overdose of a drug or intoxicant. The patients stayed in the hospital from one day to 286 days with 50 percent staying 30 days or less.

Minnesota Multiphasic

The first valid two-digit code of the Minnesota Multiphasic Personality Inventory is routinely tabulated on the IBM record of all patients admitted to the psychiatric service. All but 14 of our records had valid profiles recorded in the two-digit system. Using the "Physicians' Guide to the Minnesota Multiphasic Inventory" by Good and Brantner¹⁵ as our authority, we recorded the frequency of the two-digit codes in Table 2. Distinct analysis of each code is not the purpose of this paper but one is referred to Good and Brantner for their excellent coverage of this material. Of the valid two-digit codes, 29 cases would be equally associated with a diagnosis of either psychosis or neurosis ac-

cording to Good and Brantner.¹⁵ Briefly, however, we find that scale 2 of the Minnesota Multiphasic Personality Inventory or the scale related to the various depressive syndromes was the highest score in 22 of the patients. Nineteen patients had the highest score on scale 4 which is the scale derived chiefly from patients diagnosed as psychopathic personality, amoral and asocial type. In these patients, lying, stealing, alcohol or drug addiction, and sexual immorality are the most frequent digressions from the moral code. Fifty-two patients, or 74 percent of the total number of valid Minnesota Multiphasic Personality Inventories in our study, had either a high 2 scale or a high 4 scale as a predominant feature.

Suicide Attempt

We found that of the 84 patients, 26 (31 percent) had made previous suicide attempts and that 11 (13 percent) had a diagnosis of psychosis recorded some place in their records.

Drugs Abused

A detailed history of all the drugs the patients had abused was not routinely recorded by our physicians. Most probably, the patient was not able to or was unwilling to identify all of the drugs he had taken. We found the

TABLE 2
First Valid MMPI Two-Digit Codes¹⁵

Code	Number
12-21	4
13-31	3
23-32	4
24-42	12
26-62	3
27-72	8
34-43, 36	2
39	1
46-64	3
47	4
48-84	6
63-36	1
67	2
68-86	3
69	1
78-87	2
79	1
82-28	4
83	2
94-49	2
98	2

*See Test Your Word Score Page 221.

sedative group of drugs was the most frequently abused in the drug addictive group (see Table 3). Common barbiturates were recorded in 33 of the 84 records and were the most frequently recorded drugs, while minor tranquilizers were recorded abused in 23 records. Codeine preparations on the narcotic drug list were the most commonly abused narcotic drug, with 10 instances recorded. Stimulating drugs were often used in combination with sedative drugs, but we

TABLE 3
Drugs "Abused" List

Sedative Drugs	Incidence on Records
Common Barbiturates	33
Non-barbiturates	13
Chloral Hydrate	2
Bromides	1
Total:	49
Minor Tranquilizers	
Meprobamate	19
Diazepam	1
Chlordiazepoxide Hcl	3
Total:	23
Narcotic Preparations	
Codeine preparations	10
Meperidine Hcl	3
Morphine	3
Hydromorphone Hcl	2
Total:	18
Stimulating Compounds	
Amphetamine-like compounds	15
Stimulant-sedative combinations	3
Methylphenidate Hcl	1
Total:	19

TABLE 4
Drug Withdrawal Methods

	No. Patients	No. Seizures
1. Patients on seizure control drugs	19	0
(a) abrupt withdrawal	7	0
(b) gradual withdrawal	12	0
(c) on phenothiazine derivatives	7	0
(d) not on phenothiazine derivatives	12	0
2. Patients not on seizure control drugs	25	6
(a) abrupt withdrawal	23	6
(b) gradual withdrawal	2	0
(c) on phenothiazine derivatives	10	3
(d) not on phenothiazine derivatives	15	3

found multiple abuse of drugs in various combinations.

Disposition

The final disposition of our 84 patients was as follows: nine left against medical advice, two were committed to psychiatric services, two had to be transferred to other wards for medical or surgical reasons, 69 patients received regular discharges and two patients received "other" type discharges. Although continued care was recommended by the physicians on disposition, only twice did they go to the point of commitment. In 13 cases there was no recommendation for follow-up care. For the others continual care was recommended.

Management

Current practice in our hospital includes the use of anti-convulsant therapy in drug withdrawal. Nineteen patients received anti-seizure medications during the time of drug withdrawal (see Table 4).

Anti-Convulsant Drugs

Anti-seizure medication used was either diphenylhydantoin, 16 cases, mephobarbital alone in one case, and a combination of these drugs in two cases. Of the nineteen patients receiving seizure control drugs, none had seizures, while six patients had seizures while being withdrawn without seizure control drugs.

Since phenothiazine drugs are suspected of producing seizures,^{16,17} we recorded the use of these drugs during drug withdrawal (see Table 4). Seven patients on both phenothiazines and anti-seizure drugs had no seizures, while of the nine patients on phenothiazines alone, three had seizures reported during withdrawal. The other three who had seizures were not receiving phenothiazine drugs.

Rate of Withdrawal

Another factor that seems important in the management of drug addiction is the rate of withdrawal from the drug of addiction. In our series, 30 of the patients were withdrawn abruptly while 14 patients were

withdrawn gradually. All six of the patients who had seizures on drug withdrawal were being abruptly withdrawn.

A review of medical management during withdrawal of alcohol produced similar observations. Nineteen of the patients received phenothiazines, while 21 did not. Anti-seizure medication was given to seven patients while 33 did not receive this type of medication. The two patients who had seizures were on phenothiazines and were not receiving anti-seizure medication. All of the alcoholic patients were abruptly withdrawn.

Discussion

The incidence of addiction (7.5 percent) in the patients admitted to our psychiatric unit is a reasonably accurate picture of our experience. A careful search of the records revealed only eight instances of failure to record the diagnosis of addiction on both of the routine record systems kept for each patient. In the patients carrying a diagnosis of addiction, there appeared to be no attempt on the part of the physicians to hide the diagnosis out of empathy for the patients, and the patients were actively treated for addiction with apparent recognition by the physician that addiction was a primary problem for them. However, errors such as failure to recognize addiction problems based on factors related to the physician's personality or to special characteristics of the patient are not accounted for and the rate of 7.5 percent must be regarded as the minimum.

Socioeconomic Status

The patients came from rural and metropolitan areas, and all social and financial classes were represented without any indication that addiction is a special problem either geographically or socially. The seriousness of the illness is most manifest in the chronic nature of addiction with three-fourths of our patients having received previous treatment.

Character Disorders

Factors of depression or character disorder were of major importance in 74 percent

of the patients with valid Minnesota Multiphasic Personality Inventories. Severe personality adjustment problems are suggested by history of suicide attempts in 31 percent of the cases and also by a diagnosis of psychotic disorder on previous admissions in 13 percent of the patients.

Addicting Drugs

The common barbiturates were recorded abused in 33 cases and were the most frequently abused drugs. However, the newer nonbarbiturate sedatives and minor tranquilizers were recorded in 36 cases. This indicates that the newer tranquilizing agents and nonbarbiturate sedatives are of major importance in the problem of drug abuse. When one considers the relatively short time that the tranquilizers have been on the market as compared with the barbiturates, equal caution seems indicated in the use of these particular drugs. Certainly an assumed safety factor of a new drug being non-addicting is one that cannot be considered valid in the treatment of people with chronic neurosis or personality difficulties or with a previous history of addiction.

Codeine preparations, perhaps because they are so readily available in cough mixtures and salicylate pain-killing combinations, are the most commonly abused narcotic preparations. Support of legislation requiring that narcotic cough preparations be sold only on prescription seems indicated.

Non-addicting Antidepressant Drugs

The major phenothiazine tranquilizers and the tri-cyclic and monoaminoxidase inhibitor-type antidepressants do not appear on the list of drugs abused by our patients. This would seem to indicate that these drugs have little appeal to the addictive patient and, therefore, may be a more appropriate choice for the treatment of anxiety and other functional problems encountered in patients with a history of addiction.

Abrupt Withdrawal vs. Gradual Withdrawal

Six of the patients being withdrawn from drugs had grand-mal convulsions during their withdrawal. In surveying the methods

of treatment during withdrawal, these patients have two factors in common: (1) they were all abruptly withdrawn from their drugs, and (2) none of these patients were receiving anti-seizure medications during the time of their seizures. In comparison, 14 patients were gradually withdrawn and, of these, 12 received anti-seizure medication with no seizures recorded. Although this sample of patients is too small to give significant statistical differences, it appears that abrupt withdrawal of the drug of addiction is hazardous, and gradual withdrawal should be routine in the treatment of drug addicts. The use of anti-seizure medication in the management of drug withdrawal is controversial, and since studies thus far have not been conclusive enough to influence clinicians, the use of anticonvulsants in drug withdrawal needs further study. If phenothiazine drugs aggravate seizure proclivity during drug withdrawal, their effect does not appear to be dramatic. Possibly, phenothiazine drugs are safe to use provided anticonvulsant treatment is given concomitantly.

The wide variety of final dispositions on

discharge from the hospital (see Table 1) indicates a serious difficulty in achieving satisfactory follow-up care for the chronic addict. It appears that the medical profession needs to re-evaluate attitudes toward addiction, particularly in regard to post-hospital treatment.

Summary

Addiction to drugs or alcohol was the primary diagnosis in 7.5 percent of the patients admitted to a general hospital psychiatric service. Analysis of these records shows that addiction exists in all social, cultural and financial strata. Addiction in these patients is characterized by its chronic nature and is accompanied by serious personality and emotional disturbances. The abuse of minor tranquilizers and non-barbiturate sedative drugs was found to be of major significance in the problem of addiction. Gradual withdrawal of the drug is recommended to prevent complications in treatment. Controlled studies on the effectiveness of anti-seizure medication during drug withdrawal are needed.

References

1. Rathod, N. H.: Epidemiological Studies in Alcoholism: A Plea for Research. *Public Health* 78:181, 1964.
2. Schremly, J. A., and Solomon, P.: Drug Abuse and Addiction: Reporting in a General Hospital. *JAMA* 189:512, 1964.
3. Blane, H. T., Overton, W. F., Jr., and Chafetz, M. D.: Social Factors in the Diagnosis of Alcoholism: I. Characteristics of the Patients. *Quart J Stud Alcohol* 24:640, 1963.
4. Essig, C. F.: Addiction to Non-barbiturate Sedative and Tranquilizing Drugs. *Clin Pharmacol Ther* 5:334, 1964.
5. Kelman, H.: Addiction to Innocuous Drugs. *Medical Times*, February, 1965.
6. Committee on Alcoholism and Addiction, and Council on Mental Health: Dependence on Barbiturates and Other Sedative Drugs. *JAMA* 193:673, 1965.
7. Fraser, H. F., Shaver, M. R., Maxwell, E. S., and Isbell, H.: Death Due to Withdrawal of Barbiturates. *Ann Intern Med* 38:1319, 1953.
8. Swanson, L. A., and Okaka, T.: Death from Withdrawal of Meprobamate. *JAMA* 184:780, 1963.
9. Berger, H.: Addiction to Methyprylon. *JAMA* 177:63, 1961.
10. Evaluation of Dependence Producing Drugs, WHO Scientific Group. WHO Techn Rep Series 287:3, 1964.
11. Blachly, P. H.: Procedure for Withdrawal of Barbiturates. *Amer J Psychiat* 120:894, 1964.
12. Pearson, M. M., and Little, R. B.: The Treatment of Drug Addiction: Private Practice Experience with 84 Addicts. *Amer J Psychiat* 122:164, 1965.
13. Wilhoit, W. M. C.: Treatment of Acute Alcoholism and Delirium Tremens. *J Florida Med Ass* 52:254, 1965.
14. Hollingshead, A. B.: Two Factor Index of Social Position. New Haven, August B. Hollingshead, pp. 2, 1957.
- 15-17 May be secured from the author or the reprints.

Anything Else?

A pulsating aorta may mean neurasthenia, thinness, anemia, exophthalmic goitre, aortic insufficiency, aneurism, dilatation, or tumor. — Osler

Wringer Injuries

Still
a
Serious
Problem*

JAMES A. GARRICK, M.D.**
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A NEGLECTED wringer injury can be a horrible sight. The patient may be seen from seven to 30 days after being injured and presents with a necrotic, infected, draining upper extremity. Tendons, nerves, blood vessels, muscles, and bones are exposed. He is toxic, and his hand, functionless.

During the lifetime of the young physician, the wringer injury has been born, has risen to its apogee,[†] and then has been all but forgotten. Orthopedic and surgical residents have been told repeatedly to be careful of prognosticating about wringer injuries and that wringer injuries are bad injuries to treat.

The first electric wringer-washer was marketed in the late 1920s. By 1932 there were more than 200,000 of these appliances in use. This figure steadily rose until the late 1940s when the electric spin-drying washer became popular.

Our ancestors who dried their clothes in the sun by laying them on the grass had no problems with wringer injuries. They washed and rinsed the clothes by beating them on rocks at the riverside, and although hard on fabrics, this method offered little danger to the washer or her observing children. But not everyone had a readily accessible rocky creek bed for washing and a grassy field for drying; so, as washing facilities moved into the basement, clothing was wrung out by hand—an inefficient but innocuous method that caused only an occasional humeral epicondylitis or exacerbated a carpal tunnel syndrome.

Soon washtubs grew a remarkable appendage called the “hand wringer,” which was much more efficient but still not sophisticated enough to be dangerous. When the

*Prize essay at the meeting of the Minnesota Surgical Society, Rochester, Minnesota, May 6, 1966. Also presented as a seminar while Dr. Garrick was on assignment at Gillette State Hospital for Crippled Children, St. Paul, Minnesota, Dr. John H. Moe, chief of staff.

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†See Test Your Word Score Page 221.

housewife caught her finger (or her child's) in the hand wringer, she needed only to reverse cranking to limit injuries to subungual hematomas. With the advent of the electrically-powered wringer-washer, the reasonably safe hand-operated wringers were soon doomed to minute car-wash operations and service stations. Now clothing, sheets, fingers, forearms, and various other appendages could be instantly passed between two hard-rubber rollers with the mere turn of a switch.

Even the early appliances were equipped with elaborate safety devices that would automatically release with the presence of an adult hand between the rollers (thereby limiting more than 2/3 of all wringer injuries to children less than 10 years old).¹ However the hand of the two-year-old has approximately the same thickness as a double layer of duofold underwear, and a machine that would release automatically with anything thicker than a linen handkerchief would hardly be practical.

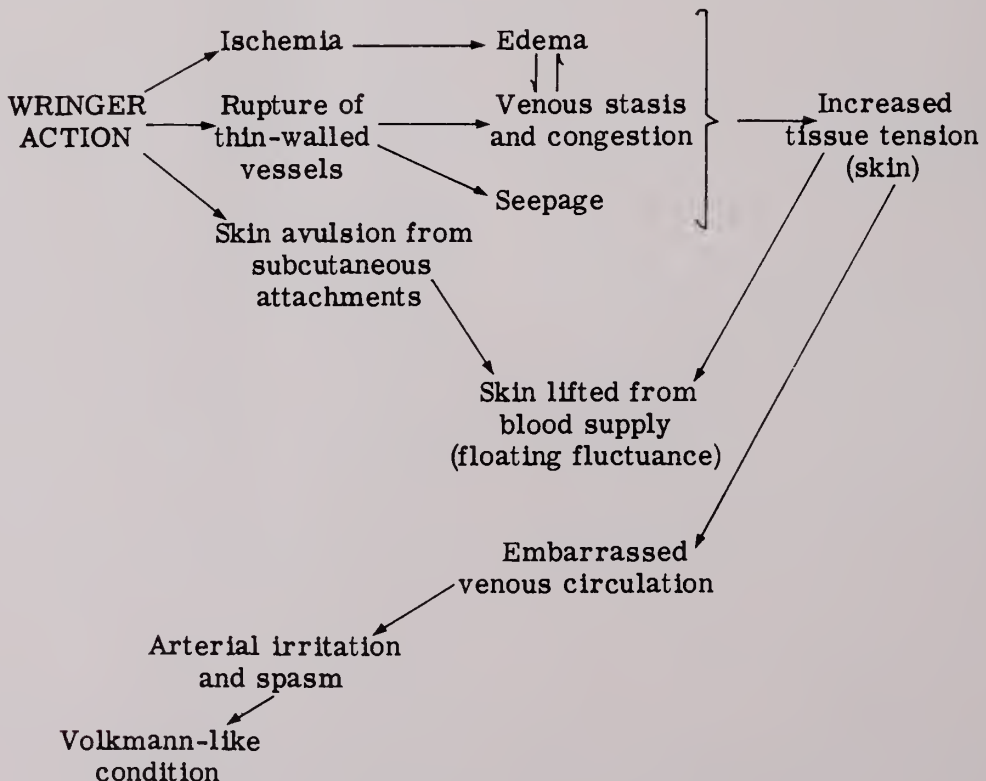
And so developed the "innocent-looking" wringer injury. Since MacCollum's² descrip-

tion (and naming of the injury in 1938), there have been more than 50 papers published dealing with this subject, many of which have obviously been ignored. If such were not the case, the neglected wringer injury would be nonexistent.

Pathologic Features (Figure)

The mechanism of injury is obvious. Who hasn't watched a child observe with rapt attentiveness the disappearance of pieces of clothing between the rollers of a wringer. The temptation to "touch" or "help the clothes go through" is often too great in spite of mother's repeated warnings. Once pulled into the wringer, the panicky child does not have the presence of mind to strike the release lever even if he were able to reach it. So the excursion of his extremity through the wringer stops only as a bony block is reached (that is, the abducted thumb, the elbow, or the axilla)³ and the soft tissue is ground away until help appears.

Unfortunately, the problems often are compounded at this time. Most mothers, con-



Schematic diagram of pathologic sequence in wringer injuries.

fronted by a screaming child with portions of his upper extremity protruding from either side of a wringer do not do the most logical thing by simply releasing the safety catch. They either jerk the arm out against the pull of the moving rollers, stop the rollers and then extract the extremity against stationary rollers, or they may simply reverse the rollers and "wring the arm out" as it were, so the child suffers a crushing injury going in and a tearing injury coming out.² It is indeed fortunate that the sight of a child with his arm in a wringer is such a horrifying one that most mothers immediately rush the child to a physician.

Avulsion of Soft Tissues

The primary injury involved is an avulsion of skin from its subcutaneous attachments. The subcutaneous fat is torn from its superficial and deep attachments, giving rise to crepitation on palpation. As a result of temporary ischemia caused by the wringer itself, edema of all tissues is the hallmark of the first 24 hours. Edema is also increased by venous stasis secondary to the rupture of thin-walled venules.

Minimal-to-moderate bleeding into the soft tissues also occurs early but is usually the result of seepage from multiple ruptures of small vessels and not from a loss of continuity of major vessels. The edema and venous congestion cause increasing tension on the tissues, particularly the skin, which, if unchecked, is lifted from its attachments and thereby from its blood supply. This phenomenon gives rise to the sensation of "floating fluctuance" encountered on palpation.⁴

Vascular Injury

Still greater increases in subcutaneous edema and bleeding not only continue to embarrass venous circulation but also cause arterial irritation and ultimately arterial spasm, thus yielding a Volkmann-like condition.

The generalized venous stasis leads to an equally generalized inflammatory response of all involved tissues, which usually begins within the second 24 hours. At one week,

the inflammatory response is replaced by proliferation of connective tissue which leads to the contractures that are so often seen.

With the typical wringer injury (that is, one without open flaps, deep or extensive lacerations, or fractures) the subcutaneous tissues suffer most, because it is within this plane that the tissues separate. Lacerations are relatively rare (seen in only 10% of the injuries). Free-flap avulsions are more common.

Skin necrosis is usually most extensive over areas likely to accumulate collections of subcutaneous fluid, such as the palm of the hand and the antecubital fossa, or skin surfaces overlying bony prominences such as the styloid processes and the humeral condyles where there is no subcutaneous cushion to absorb the crushing force of the rollers.

Bone Injury

Fractures are rare, occurring in only 2 to 4% of the cases.¹ When present, fractures usually are nondisplaced and often are of the greenstick variety. Unless the fracture site is open by virtue of an overlying flap avulsion, fractures do not offer much of a problem in management.

Soft Tissue Injury

Damage to tendons, nerves, or major blood vessels is a rarity in the typical wringer injury.⁵ When these structures are injured, it is generally a result of unrelieved pressure from the accumulation of subcutaneous and deeper fluids.

Typical damage to muscle consists of micro-hemorrhages. Rarely are muscles per se torn. Not infrequently the muscle, complete with its fibrous envelope, is torn loose from adjacent tissues although it may remain attached at its origin and insertion.⁶ On rare occasions, intramuscular hemorrhage will be extensive enough to merit incision and drainage.

The problems resulting from this type of injury are legion in spite of the small number of tissues that initially are appreciably damaged. Minimally damaged tissues heal

very slowly if the damage is caused by a crushing force. The arterial supply to these tissues usually is adequate at first, but the venous return is grossly inadequate. Also because of the poor circulation, the local tissue resistance to infection is poor.

If the injured site is contaminated, as in the case of lacerations or abrasions, the contaminants usually are easily controlled with standard antibiotic therapy. However, the necrotic or improperly treated wound that has been allowed to become infected often results in a functionless extremity and even in amputation.

Diagnosis

Although the victim invariably is seen early by a physician, treatment in many of these injuries is inadequate. In the neglected wringer injury the typical history is one of the child being seen early in the physician's office or in an emergency room, with very little damage being noted on physical examination (usually there is not much more to see than a slight swelling and abrasions during the first few hours). The inevitable roentgenograms are taken and show nothing abnormal. The child is then sent home and advised to rest his arm.

Since the final outcome of these injuries is all but impossible to predict, a prognostication should never be attempted. However, the physician should have some idea of the probable extent of damage in order to institute the proper treatment. Therefore, it is important to know how the child was extracted from the rollers, how long he was caught in the wringer, how tightly the rollers were set, how much time had elapsed since the injury, as well as the age and size of the child. Surprisingly enough, young children generally have less severe injuries than do older ones, because of the greater elasticity of their tissues and the smaller size of the extremity.

Initial inspection is of value. The presence of blotchy, ecchymotic skin shortly after the accident is an ominous sign, as it signifies potential areas of necrosis. Determining the function of the extremity is of little value, because generally the child is unwilling to

cooperate. It is well accepted that, in injuries of a crushing type, loss of function need not parallel damage (or potential damage) to the extremity.

Although fractures are rare in wringer injuries, initial roentgenograms should always be taken. Because of the extensive damage to soft tissue adjacent to tendons, which often leads to fibrosis and dysfunction of these tendons, fractures when present are slow to heal.

Treatment

The basic premise in the treatment of wringer injuries is to achieve primary healing by means of massive compressive dressings.

First Aid

Immediate first aid should consist of application of a voluminous pressure dressing that is evenly applied, as well as splinting and elevation of the extremity. No attempt should be made to determine the full extent of the injury; the time required to evaluate the injury should be used to transport the patient to a physician.

Antiseptic Procedures

The entire involved extremity should first be gently washed with a hexachlorophene soap and soft-gauze fluffs (never a brush). Whether or not the wound is open, the washing should be carried out under sterile conditions with the operator gowned, masked, and gloved. A second 5-minute scrub with sterile water, sterilized soap, and a change of gown and gloves for the operator should follow. Since the initially unbroken skin may break down soon after the accident, future contamination may thus be prevented.

Surgical Procedures

After the wound is cleansed, any laceration should be thoroughly irrigated and closed primarily.⁷ Only obviously nonviable tissues should be debrided. Jagged edges should be dovetailed but not trimmed for cosmesis. This initial treatment is aimed at closing the wounds and not at restoring full

function. Attempts at plastic-type closures involving rotating skin flaps, Z-plasty, and so forth are ill-advised because excessive handling might compromise the already precarious blood supply to the ischemic tissues.

Suturing should be carried out as soon as the tissues have been cleansed and debrided. Any swelling causes retraction of excessive skin and subsequent difficulty in closure without undue tension. Flaps that have been doubled back to allow access to deeper tissues develop edema rapidly because of the kinking of already damaged veins.

Grafting

Opinions are many and varied regarding the handling of large avulsion flaps. Some physicians recommend suturing the entire flap in place regardless of questionable viability and utilizing the flap as a large pedicle, stating that much of the skin will live in spite of considerable infection.⁸ This technique invariably involves secondary grafting procedures after the infection that usually develops is controlled. To expect a pedicle graft of ischemic, crushed skin (even though well cleansed and defatted) to survive in an edematous, congested, recipient site requires faith of rather heroic proportions.

A second group suggests debriding all tissues of questionable viability, closing what skin remains, and covering the remaining open areas with split-thickness grafts at the initial treatment. Many of the advocates of this method clean and defat open flaps (and even circumferential ones) and use them as the grafting material. Opponents of this practice contend that (1) much of the debrided skin is damaged too much to function ideally as a graft; (2) the procedure takes too long; (3) attempts at placing grafts on a surface that has not become "naturally" hemostatic is asking for the graft to be floated off by pooling blood; and (4) fresh normal skin is readily available with an electric dermatome, a procedure best done seven days after the injury. Hence these critics advocate closing as much viable skin as possible, covering the remaining open areas with an appropriate dressing, and carrying out split-thickness grafting procedures five to seven days later.

Nearly every physician agrees that the use of a primary pedicle-type graft is ill-advised because of the operator's inability to distinguish viable from nonviable tissue and, therefore, because of increasing the possibility of suturing the pedicles to already

Summary of Do's and Don'ts in Treatment of Wringer Injuries

	Do	Don't
Cleansing	Use sterile technique (mask, gown, gloves) Be gentle	Use a brush
Closure	Debride only the obviously nonviable tissue Dovetail jagged edges Work rapidly Grafting procedures in 5 to 7 days Immobilize unstable fractures Reapproximate trimmed nerves	Trim for cosmesis Undertake split-thickness graft immediately Attempt pedicle flaps Primarily repair tendons Use a tourniquet
Dressing	Dress with nonadherent dressings, longitudinally placed 4- by 8-inch gauze sponges, evenly applied gauze fluffs, circumferentially applied cellulose bandage (Curlex), or nonrubber elastic bandage	Use "mechanic's waste" Use rubber elastic bandages
Immediate after-care	Elevate the extremity Administer tetanus toxoid or hyperimmune globulin	Use heat
Later care	Aspirate when there is any sign of subcutaneous pressure buildup Incise and drain if aspiration does not immediately relieve pressure	

doomed skin. The practice of placing a hand, denuded of skin, under an abdominal flap is also generally condemned, because retaining a functional position for the hand under these circumstances is all but impossible.

Tourniquet Not Indicated

Regarding skin viability and grafts, there is one point of almost universal agreement: that the use of tourniquet during cleansing, debridement, or at any time during the early treatment of wringer injuries is one of the surest possible ways to increase the already present ischemia.

Dressings

Superficial "brush-burn" abrasions should be cleansed and covered with an appropriate dressing. Some physicians recommend the use of tulle gras, which is paraffined, coarse-meshed gauze, impregnated with petrolatum, 1% tincture of benzoin, and 1% balsam of Peru. Others use gauze impregnated with a combination of scarlet red and petrolatum. Still others use a sterile fine-meshed gauze soaked in saline or a nonadhering commercially available dressing such as Adaptic.

Nerves, if divided, should be minimally trimmed and reapproximated to decrease scarring by being sutured through the perineurium. Definitive repair may be carried out at a later date if necessary.

Care of Injured Tendons

Tendons should be excised only if they are shredded beyond repair. Primary tendon repair is generally held in disfavor as it appreciably lengthens the operation and causes an increased extravasation of blood and fluid while the severed ends are being hunted and mobilized. Such repair also increases the likelihood of skin-flap necrosis if additional incisions are required to find and mobilize the proximal tendon fragments. Even if attempted, primary tendon repair is often doomed to failure because tendons, which are normally slow healing, heal even more slowly after a crushing injury.

Management of Fractures

Unstable fractures, which are rare, require immobilization if for no other reason

than to prevent further damage to soft tissue. When fractures are unstable, they are generally open as well; but in spite of this, internal fixation, although not ideal, is the treatment of choice. Often this can be accomplished by the use of wire sutures or Kirschner wires for small bones of the hand, the ends being placed subcutaneously and not brought out through the skin. Under no circumstances should plaster casts be used during the initial phases of treatment of wringer injuries.

Compression Dressings

After wound closure all sutured and abraded areas are covered with small overlapping strips of the dressing material. Next four-by-eight inch gauze sponges are applied longitudinally, followed by evenly applied gauze fluffs. The use of "mechanic's waste" is becoming unpopular because of the difficulty of applying this material evenly enough to achieve uniform compression.⁹ A cellulose-type gauze (Curlex) is next applied circumferentially, and this in turn is covered by a nonrubber elastic bandage. The use of rubberized elastic bandages can lead to excessive compression. Care must be taken to eliminate dead spaces, such as those that occur in the palm and result from lateral compression and cupping of the hand. Excessive compression may be alleviated by the placing of a mass of steel wool in the palm in the gauze-fluff layer of the dressing or by the suturing of the dressing through the hand. The sutures are brought out on the dorsum and are tied over a piece of felt or padded button. The affected extremity should then be elevated and the circulation of the finger tips checked almost constantly.

Cooling of Tissue

The use of heat to the involved extremity is also to be condemned; however, cooling of the extremity decreases the metabolic rate of the damaged tissues and may well be the determinant factor in the survival of the skin and deeper tissues. One of the new, smaller cooling blankets can be incorporated into the dressing, just superficial to the layer of gauze fluff; this serves not only as an ad-

ditional splinting material but also as a means of decreasing the temperature of the extremity.

Even if no open wounds are present at the initial treatment, the patient should be given tetanus prophylaxis. The newer hyperimmune human antisera negate most of the problems seen previously with horse serum.

The time lapsing before the first change of dressing and the examination of the extremity varies. Some physicians recommend that the extremity should be inspected every 12 hours until the exact status of the wound can be ascertained. Others report equally good results by changing the initial dressing two to three days after the injury and then seeing the victim on an outpatient basis. The victim is admitted to the hospital only in the event of gross tissue necrosis or mass swelling in spite of compression dressings.

Incision and Drainage

However, all agree that if there is any evidence of a subcutaneous pressure buildup when the first dressing is changed, aspiration should be immediately attempted; and if this does not alleviate the pressure, then

incision and drainage must be carried out.

When incision and drainage are necessary, longitudinal incision is made to the level of the fascia, as the majority of the fluid collections are external to the fascial layers. If the underlying muscles still seem under undue tension, the fascia enveloping the muscles must also be incised. After drainage, the fascial layers are not closed, but the skin is loosely approximated without tension and the compression dressing reapplied. With this method, there is no necessity for repeating the incision and drainage procedure in the same area.

Summary

Proper early care of a wringer injury requires little more than strict adherence to accepted surgical principles which include cleansing and debridement, primary skin coverage, the use of compression dressings, adequate immobilization, and careful observation.

Wringer injuries will ultimately follow the wringer-washer into history and "neglected wringer injuries" should precede this appliance into antiquity.

References

1. Iritani, R. I., and Siler, V. E.: Wringer Injuries of the Upper Extremity. *Surg Gynec Obstet* 113:677, 1961.
2. MacCollum, D. W.: Wringer Arm: A Report of Twenty-six Cases. *New Engl J Med* 218:549, 1938.
3. Posch, J. L., and Weller, C. N.: Mangle and Severe Wringer Injuries of the Hand in Children. *J Bone Joint Surg.* 36-A:57, 1954.
4. MacCollum, D. W., Bernhard, W. F., and Banner, R. L.: Treatment of Wringer-Arm Injuries. *New Engl J Med* 247:750, 1952.
5. Allen, H. S.: Wringer Injuries of the Upper Extremity. (Abstr.) *Ann Surg* 113:1101, 1941.
6. London, P. S., and Clarke, R.: Severe Accidental Flaying: A Plea for Initial Conservatism. *J Bone Joint Surg* 41-B:658, 1959.
7. Bell, J. L., Mason, M. L., and Allen, H. S.: Management of Acute Crushing Injuries of the Hand and Forearm Over a Five-Year Period (1948-1952). *Amer J Surg* 87:370, 1954.
8. Farmer, A. W.: Treatment of Avulsed Skin Flaps. *Ann Surg* 110:951, 1939.
9. Hausmann, P. F., and Everett, H. H.: Wringer Injury. *Surgery* 28:71, 1950.

Medical Men on Postage Stamps*

Hermann von Helmholtz (1821-1894), German anatomist and physiologist of the eye, the ear, and the nervous system, inventor of the ophthalmometer, and author of scientific works on physiological optics and acoustics, was memorialized on a postage stamp issued by Germany in 1950.

Crawford Long (1815-1878), American surgeon, who claimed to have performed the first operation with the patient anesthetized by ether (1842), received recognition for his pioneer achievement on a U. S. postage stamp issued in 1940.

*See *Minnesota Med* 49:1930, 1966.

The Doctrine of Signatures

According to this doctrine nature has placed upon natural objects in general (animals, plants and minerals) a sign, or marking, or has given them a symbolic appearance, to indicate their special usefulness for the treatment of certain maladies or for the diseases of certain organs. Some of the keenest minds of the past centuries accepted this doctrine with no apparent difficulty.

Like cures like, that is the principle underlying the doctrine. Therefore a plant with a leaf shaped like a kidney, would be good for kidney trouble, hence the kidney wort. We have also the liverwort, because its leaf is seemingly shaped like the liver. Frequently the supposed signature (i.e., the resemblance) was far-fetched indeed, as for example, in the case of the tough gelatinous fungus, known for centuries as the Jew's ear which was used as a cure for ear complaints.

Erysipelas, because it is accompanied by a bright-red, feverish rash, was treated with red things — red pepper, cranberries, and red flannel. In small-pox red bed-coverings were used to bring the rash to the surface. When Edward II (1284-1327) King of England had small pox his physician, John of Gaddesden, directed that everything about the room, the dresses of the patient and attendants, the bedding and furnishings should be scarlet. Four hundred fifty years later, when Francis I (1708-1765) emperor of Germany had small pox, he was treated in a similar manner.

Avicenna (890-1037 A.D.) the renowned Arabian physician was convinced that because the blood is red, substances which are red in color must be used in treating diseases of the blood. Nine hundred years after Avicenna doctors were ordering red wines for patients poor in blood, and white wines for those whose "blood was too rich."

We know now that the Doctrine of Signatures is just the veriest nonsense. Whatever benefits were derived by such beliefs resulted merely from the power of suggestion.*

*Thomen, A. A., M.D.: *Don't Believe It! Says the Doctor*, Blue Ribbon Books, New York, 1935.

On the Art of Medicine

Medicine is both a science and an art. . . . It is an art when it becomes necessary to apply it to a human being who is ill, and this is especially true when the manner of treatment is under consideration. It is in this art that the physician reveals how much talent he possesses; he reveals himself as a true artist by the particular form of remedial preparation which he decides to administer to his patient, by the felicitous choice which he makes between remedies, and by the favorable manner in which he combines them. — Armand Trousseau (1801-1867)

Heart Symposium

Symposium on Emotions and Heart Psychophysiology of the Coronary Heart Disease Patient sponsored by L. E. Phillips Psychobiological Research Division of North Memorial and Mount Sinai Hospitals in conjunction with the Minnesota Heart Association, Sunday, April 2, 1:30 p.m., North Memorial Hospital Auditorium, Minneapolis, Minnesota.

Massive Upper Gastrointestinal Bleeding

Caused
by
Aortojejunal
Fistulization

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AORTOENTERIC FISTULIZATION producing massive gastrointestinal bleeding has been reported with increasing frequency as a delayed complication of abdominal aortic aneurysm resection and grafting.

Including three previous cases known to the authors, 84 cases collected from the literature^{1,3,4,5,6,7,8,9,10,11,12} and the case to be described, a total of 88 patients were found to suffer from this lesion.

The occurrence rate of aortoenteric fistulas following abdominal aortic surgery is between 0.3 and 5 per cent.^{7,5} In 80 per cent of cases fistulization is into the distal duodenum or into the proximal jejunum in the remainder.

The average time for development of a fistula is 24 months for homografts and six months for synthetic prostheses. The explanation for this discrepancy probably lies in the tendency for gradual disintegration of the central portion of the homograft, the area where most homograft fistulas occur (80%). In theory, no such degeneration develops in teflon and dacron prostheses. Therefore, when fistulization does develop with this type of prosthesis it is most likely related to technical problems at the proximal suture line and will occur early. The grafts employed in the collected group of 88 patients are listed in Table 1. Homografts predominate and will probably continue to be the source of fistulization in a significant number of patients in the future.

Diagnosis

Gastrointestinal Bleeding

The diagnosis of aortoenteric fistula⁵ rests mainly on obtaining a history of previous abdominal aortic surgery in a patient with gastrointestinal bleeding. A pulsatile abdominal mass is confirmatory evidence in a minority of patients. It is our opinion that in the actively bleeding patient laparotomy should be performed as soon as feasible and

the presumptive diagnosis substantiated or refuted by exposing the previous operative area.

Massive Melena

Gastrointestinal hemorrhage was present in all patients studied and in almost all hypotension and massive melena were noted. The time between onset of hemorrhage and death or surgical intervention varied from two hours to eleven months. However, experience has shown that only a relatively small portion of these patients will die as a result of the initial hemorrhage and that there exists sufficient time for surgical correction if this complication is suspected.

Causes of Failure

Technical Errors

Several technical faults which may cause aortoenteric fistulae include: faulty proximal suture line, discrepancy between the size of the host aorta and the selected graft, poor quality of proximal aortic cuff, failure to interpose viable tissue (peritoneum, omentum or aneurysm wall) between the aortic graft and the intestines, and injury to the proximal small intestine at the time of aortic mobilization. In addition, damage to the vasa vasorum* may impair healing at the proximal suture line.¹⁰

Surgical techniques must avoid these errors to prevent fistulization. Dissection of abdominal aneurysms in an intraluminal plane will preserve the outer media and adventitia, allowing this retained arterial wall to serve as an excellent anterior reinforcing

layer for the prosthesis and proximal suture line.

Local Infection

Local sepsis developing in a retroperitoneal hematoma due to faulty hemostasis will almost surely result in dehiscence of the proximal suture line. That a large retroperitoneal hematoma may itself dissect through the layers of the gut is theoretically possible. The close anatomic proximity of the distal duodenum and first portion of jejunum obligates fistulization from the aorta into this portion of the intestinal tract.

Precautions

Massive antibiotics and an osmotic diuretic should be administered intravenously as soon as the need for aortic re-resection is recognized. Resection of the entire previously placed graft appears mandatory, in spite of any technical difficulties. If necessary, a pedicle graft of omentum may be placed anterior to the new graft and interposed between it and the intestines. The problem posed when an infected proximal suture line is encountered as the basis for fistulization is almost insurmountable. It has been suggested⁶ that a portion of adherent gut along with the involved segment of aorta be resected en block to prevent reinfection of the operative area. This plan presents certain technical difficulties but should be feasible in some cases.

Results

A summary of results obtained in the 88 patients is presented in Table 2. Twenty-six patients were not operated upon; all of these succumbed to massive hemorrhage. Eight patients were subjected to non-definitive surgical procedures such as abdominal

*See Test Your Word Score Page 221.

TABLE 1
Types of Aortic Grafts (1953-1965)

Homograft	50
Dacron	21
Nylon	7
Teflon	5
Orlon	2
Unknown	3
	88

Summary of types of aortic grafts previously employed in 88 patients with aortoenteric fistulae and gastrointestinal bleeding. (collected series).

TABLE 2
Results (1953-1965)

26 patients	8 patients	54 patients
↓	↓	↓
No surgery	Non-definitive surgery	Definitive surgery
↓	↓	↓
100% mortality	100% mortality	19 survived 65% mortality

Summary of results of treatment in 88 patients with aortoenteric fistulae following previous abdominal aortic surgery. (collected series)

exploration, "blind" gastric resection or local patching of the aortic fistula; and all of these patients expired in the early postoperative period. In contrast, nineteen of fifty-four patients treated by resection and grafting survived. This represents only a 35% survival rate, admittedly less than ideal, but is in keeping with the severity of the disease. We believe that if earlier diagnosis is followed by aggressive surgical treatment, more of these patients will be salvaged.

Case Report

History

A 67-year-old white man was seen on the morning of August 28, 1965, complaining of recurring melena during the preceding twenty-four hours and of a syncopal episode immediately prior to admission. There was no significant past history of gastrointestinal complaints, abdominal pain or ingestion of drugs or alcohol. He denied intermittent claudication. In 1957 he had undergone emergency resection and grafting for a ruptured abdominal aortic aneurysm. The aorta was replaced with a nylon bifurcation prosthesis and the patient made an uneventful recovery.

Findings

Physical examination revealed a pale, anxious man who was in no pain. His heart rate was 104 and his blood pressure 70/40. The lungs were clear and there were no cardiac murmurs. There was a healed midline scar and a prominent, pulsatile mass in the mid-abdomen. A systolic bruit was heard best immediately to the left of the umbilicus. The right femoral pulse was diminished and the right popliteal and pedal pulses were absent. Rectal examination disclosed mahogany colored stool. Bright red blood was recovered from the nasogastric tube.

His hemoglobin was 11.2 gm. % and hematocrit 39. The blood urea was 29 mg. %. Other laboratory studies, including an ECG., were within normal limits.

A diagnosis of aortoenteric fistula was made and the patient prepared for surgery. He received par-enteral fluids, one unit of plasma and two units of whole blood. A Foley catheter was inserted and a central venous pressure monitor established.

Surgical Procedure

The abdomen was entered and no evidence of disease was encountered during a rapid examination of the upper gastrointestinal tract. The transverse mesocolon was elevated and dissection was begun in the region of the root of the mesentery. Several loops of proximal jejunum were tightly adherent to the area of previous aortic resection (Figure 1). After achieving preliminary proximal control by passing a tape around the aorta at the level of the aortic hiatus the coils of jejunum were carefully dissected off the aortic prosthesis. The fistula was encountered 4 cm. distal to the left renal vein. Aortic bleeding was controlled with digital pressure while further dissection allowed placement of

a proximal aortic clamp. The jejunal defect was temporarily controlled with a non-crushing clamp and later meticulously closed (Figure 2). The nylon prosthesis was densely adherent to surrounding structures, and for this reason it was elected to oversee its proximal end and leave it in place. A 16 mm. Dacron bifurcation prosthesis was then sutured to the short aortic cuff below the renal arteries and anastomosed distally as indicated in Figure 3.

Progress

His postoperative course was uneventful until the 10th day when he developed a mechanical small bowel obstruction necessitating reoperation and division of numerous adhesions. His recovery was further delayed by a prolonged period of ileus and the development of jaundice. Both gradually subsided and the patient was dismissed on the 36th postoperative day.

Disintegration of Original Nylon Prosthesis

On October 30, 1965, he was re-hospitalized com-

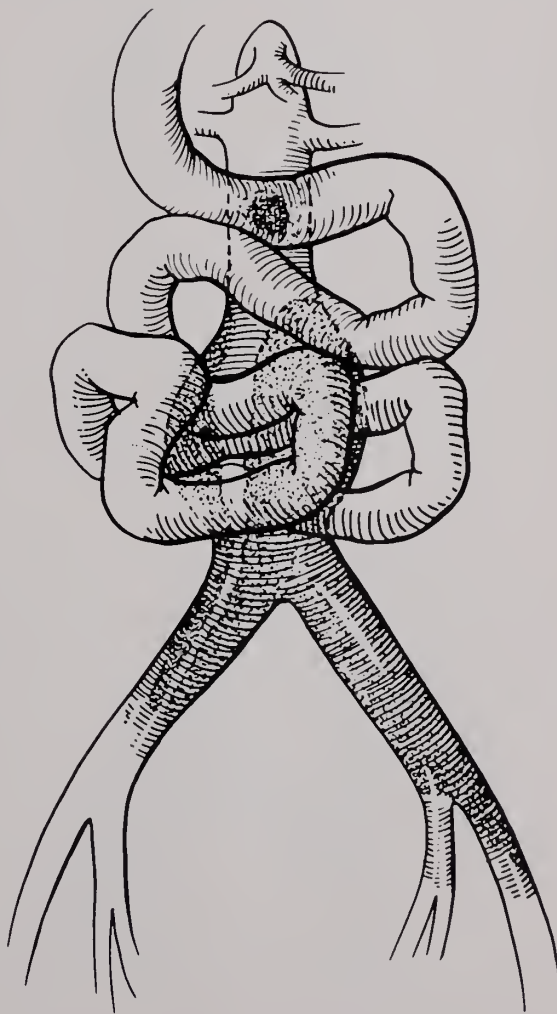


Fig. 1.— Findings at surgery. Note adherent loops of proximal jejunum in region of previous aortic surgery.

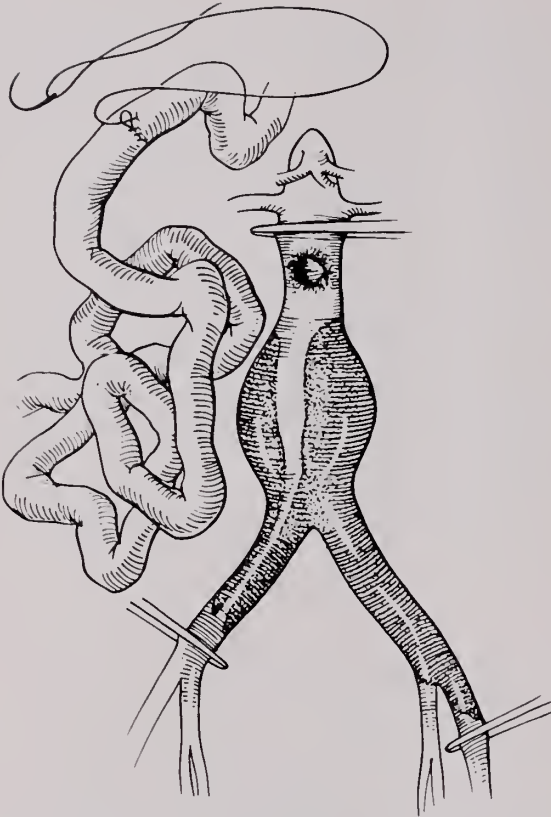


Fig. 2.—Proximal and distal aortic control and closure of jejunal defect.

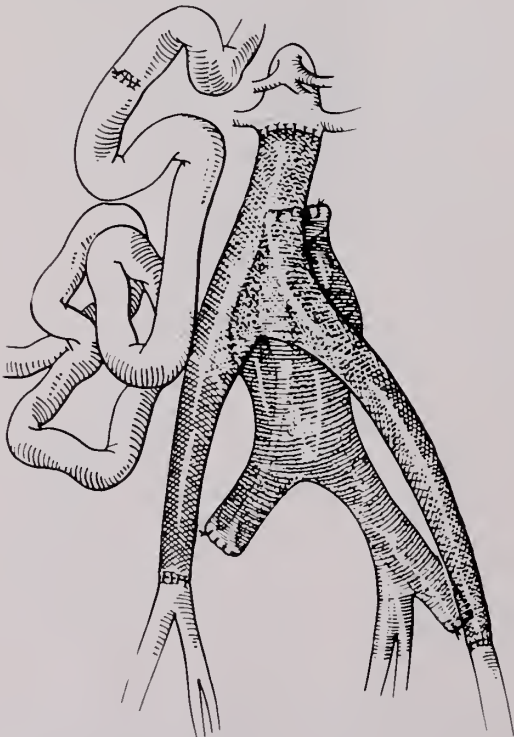


Fig. 3.—Completed anastomoses. Nylon prosthesis oversewn and left in place.

plaining of severe upper abdominal and left flank pain which had become progressively worse over the previous three days. Physical examination revealed a pale, rather cachectic man with a temperature of 100.6 F., pulse of 100 and blood pressure of 140/90. There was a 10 × 8 cm. mass in the left mid-abdomen, which was pulsatile along its medial border. No bruits were heard and the peripheral pulses were intact. Roentgenograms of the abdomen were not helpful. The white count was 15,600 with 89% PMNs. The hemoglobin was 10.0 gm. %.

A diagnosis of false aneurysm, probably arising from the proximal suture line was made, and while preparations for surgery were being completed he developed massive hematemesis and become hypotensive.

Second Operation

At surgery proximal aortic control was again obtained prior to retroperitoneal dissection. A large hematoma was encountered anterior to the dacron prosthesis which was entirely intact. There was a large defect in the proximal jejunum adjacent to the hematoma. After evacuation of the hematoma there was apparent free back bleeding from the area of the left common iliac artery where the previously placed left limb of the nylon prosthesis had been sutured in 1957 (Figure 4). Here the nylon prosthesis had virtually disintegrated, leaving a wide open defect. This area was oversewn and the nylon prosthesis was removed completely.

The patient then made steady improvement until the 7th of November when he suddenly developed signs of pulmonary infarction in the left lower lobe. He was reluctantly started on anticoagulants. On the 9th of November a mass in the mid-abdomen was noted, along with gastrointestinal bleeding and hypotension. Although the situation seemed hopeless, re-exploration was carried out and again a large posterior hematoma was encountered. The source of the bleeding could not be determined. A large defect in the proximal jejunum was again present. Closure of the bowel wall was extremely difficult because of its friability.

Following this procedure there was brief improvement, but further intestinal hemorrhage ensued and the patient expired on November 26, 1965. Unfortunately a postmortem examination was not allowed by the family.

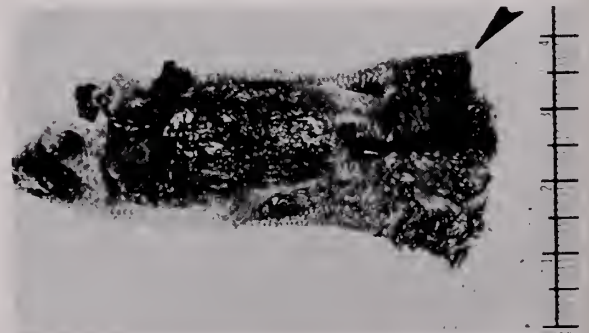


Fig. 4.—Nylon bifurcation prosthesis removed at surgery (see text). Arrow indicates site of prosthetic disintegration.

Comment

Although progressive disintegration of ivalon, nylon, orlon, amylon and polyethylene prostheses is well known,³ the particular complication of back bleeding from one of these prostheses left in situ has not been described heretofore. It is painfully clear that the further disruption of the previously placed nylon prosthesis (1957) which was not totally resected and resultant hemorrhage caused the patient's demise.

We would therefore strongly recommend that in any case of fistulization from a deteriorating aortic prosthesis it be removed from any vascular continuity regardless of technical difficulties involved.

Conclusions

From continuing disintegration of the residual nylon prosthesis this experience has convinced us that any previously placed prosthesis, be it homograft or plastic, should be removed completely at the time of corrective surgery.

Early diagnosis of aortoenteric fistulization is the key to proper therapy. It depends upon constant awareness of the possibility of this lesion developing in any patient who has had previous abdominal aortic surgery. It should be emphasized further that there is usually sufficient time to allow these patients to undergo abdominal exploration and corrective surgery.

References

1. Cordell, A. R., Wright, R. H., Johnston, F. R.: Gastrointestinal Hemorrhage after Abdominal Aortic Operations. *Surgery* 48:997, 1960.
2. DeBaakey, M. E.: in discussion of Humphries, A. W. et al.: *Arch Surg* 86:43, 1963.
3. De Weese, M. S., Fry, W. J.: Small Bowel Erosion following Aortic Resection. *JAMA* 882:179(11), 1962.
4. Garrett, H. E., Beall, A. C. Jr., Jordan, G. L. Jr., DeBaakey, M. E.: Surgical Considerations of Massive Gastrointestinal Tract Hemorrhage Caused by Aortoduodenal Fistula. *Amer J Surg* 105:6, 1963.
5. Humphries, A. W., Young, J. R., deWolfe, V. G., LeFebvre, F. A.: Complications of Abdominal Aortic Surgery. Part I: Aortoenteric Fistula. *Arch Surg* 86:43, 1963.
6. Javid, H., Julian, O. C., Dye, W. S., Hunter, J. A.: Complications of Abdominal Aortic Grafts. *Arch Surg* 85:650, 1962.
7. Kahle, H. R.: in discussion of Humphries, A. W. et al.: *Arch Surg* 86:43, 1963.
8. Levy, M. J., Todd, D. B., Lillehei, C. W., Varco, R. L.: Aorticointestinal Fistulas following Surgery of the Aorta. *Surg Gynec Abstet* 120:992, 1965.
9. MacKenzie, R. J., Buell, A. H., Pearson, S. C.: Aneurysm of Aortic Homograft Both Rupture into Duodenum. *Arch Surg* 77:965, 1958.
10. Sproul, G.: Rupture of an Infected Aortic Graft into Jejunum: Resection and Survival. *JAMA* 182:1118, 1962.
11. Tolstedt, G. E., Jesseph, J. E., Bell, J. W.: Late Intestinal Complications of Abdominal Aortic Homografts. *Surg Gynec Abstet* 116:42, 1963.
12. Osius, E. A. in discussion of Javid, H. et al.: *Arch Surg* 85:650, 1962.

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Zerobabel Endicott was the son of Governor Endicott of Massachusetts and a practicing physician in the seventeenth century in the city of Salem.

For difficult labor, he recommended that a lock of hair from a virgin half the age of the woman in labor was to be cut into small powder and dried with twelve ant eggs in the bread oven after the bread has been removed. This powder was then to be given with a quarter of a pint of milk from a red cow, or in the absence of milk strong ale could be used.

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Faith is dead to doubt, dumb to discouragement, blind to impossibility — Defender

Platitudes are among the most useful things in the world for those who know how to use them, for truth is not the worse for being obvious, undeniable, or familiar.

President's Letter Continued from page 167.

It is our obligation to foster the patient-physician relationship as much as possible and to actively discourage the patient-agency relationship whenever we can. As physicians we have already too long ignored and neglected our professional role in this area and

should not further abrogate our responsibilities.



C. G. Sheppard, M.D.
President
Minnesota State Medical Association

Junket

I shall never forget my first meal in that hospital (St. Germicide). There was quite a good deal of talk about it beforehand. My nurse kept telling me that on the next day the doctor had promised I might have something to eat. I could hardly wait. I had visions of a tenderloin steak smothered in fried onions, and some French-fried potatoes, and a tall table-limit stack of wheat cakes, and a few other incidental comfits and kickshaws. I could hardly wait for that meal.

The next day came and she brought it to me, and I partook thereof. It was the white of an egg. For dessert I licked a stamp; but this I did clandestinely and by stealth, without saying anything about it to her. I was not supposed to have any sweets.

On the occasion of the next feast the diet was varied. I had a sip of one of those fermented milk products. You probably know the sort of thing I mean. Even before you've swallowed it, it tastes as though it had already disagreed with you. The nurse said this food was predigested but did not tell me by whom. Nor did I ask her. I started to, but thought better of it. Sometimes one is all the happier for not knowing too much.

A little later on, seeing that I had not suffered an attack of indigestion from this debauch, they gave me junket . . . I know not how it may be in the world at large, but in a hospital, junket is a custard that by some subtle process has been denuded of those ingredients which make a custard fascinating and exciting. It tastes as though the eggs, which form its underlying base, had been laid in a fit of pique by a hen that was severely upset at the time.

Hereafter when the junket is passed round somebody else may have my share. I'll stick to the mince pie a la mode.

— Irvin S. Cobb: Speaking of Operation

Avoid a Northern Exposure

Hilarity and good humor, a breezy cheerfulness, a nature "sloping towards the southern side," as Lowell has it, help enormously both in the study and in the practice of medicine. — Osler

Fashions in therapy may have some justification; fashions in diagnosis have none.

— Herrick and Tyson

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Contraindications: Dextro-amphetamine sulfate: in hyperexcitability and in agitated prepsychotic states. Previous allergic or idiosyncratic reactions to meprobamate.

Precautions: Use with caution in patients hypersensitive to sympathomimetic compounds, who have coronary or cardiovascular disease, or are severely hypertensive.

Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side Effects: Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness. Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute thrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.



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Editorials

Psychiatry and Allergy

THAT THERE IS some relationship between the psyche and most allergic illness has long been recognized. However, the extent of the role of psychologic forces in their manifestations has been the subject of much debate. In regard to bronchial asthma, this relationship was given particular impetus by French and Alexander in 1941 when they proposed the hypothesis that wheezing is a form of crying and is the result of anxiety over separation from or rejection by the mother. The proof of such a hypothesis would be difficult, and presently this hypothesis is not a proven fact though it is accepted by many in the medical profession. Much work has been done attempting to prove French and Alexander's hypothesis and to describe the "typical personality" of the allergic or asthmatic individual. Groups of patients presenting at allergy or psychiatry clinics or institutionalized for various reasons have been tested with various subjective and objective personality tests. Impressions and conclusions from direct interviews have been used, and the presence of allergy has been confirmed on a few occasions by history, examination, and skin testing. The studies have often found the individual to be restricted, hostile, and rebellious towards figures of authority. Psychoanalytically the allergic patient has been described as fixated at the oral-anal level of personality development.

The patients have been said to view themselves as cynical, irritable, and grouchy. In the September issue of MINNESOTA MEDICINE Rusten and Rusten* undertook what must have been an exhausting review of the records at the Red Wing Training School. They conclude that more of the atopics committed crimes against persons and property than did nonatopics. This supports several other investigators, notably Berendregt, who feel that allergic individuals (particularly asthmatics) tend to be hostile.

As one reviews much of the work that has been done in the area of the psychological aspects of allergic disease several observations are noteworthy. First and foremost, many of the studies have not reported adequate criteria for classifying a patient as allergic or non-allergic. Often this was determined by history as given by the patient only, and there was no confirmation. Also, the types of allergy included in the "allergic" classification were only rarely mentioned. In several studies the population from which the groups were derived was heavily biased: for example, allergic patients referred to a psychiatric clinic. Few studies have been made comparing the personality characteristics of the so-called allergic group with those of another group suffering from chronic illness of comparable severity, and finally many of the studies were poorly controlled, if controlled at all. Few of the

*Minnesota Med 49:1483, 1966.

Continued

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The following is a brief precautionary statement. Before prescribing, the physician should be familiar with the complete prescribing information in SK&F literature or *PDR*. **Contraindications:** Patients with glaucoma, prostatic hypertrophy, stenosing peptic ulcer, pyloroduodenal obstruction, or bladder neck obstruction. **Precautions:** Use with caution in the presence of hypertension, hyperthyroidism, or coronary artery disease; and, in patients who may operate vehicles or machinery, warn of possible drowsiness. **Note:** Since the iodine in isopropamide iodide may alter PBI test results and will suppress I^{131} uptake, it is suggested that 'Ornade' be discontinued one week before these tests. **Side effects:** Drowsiness; excessive dryness of nose, throat, or mouth; nervousness; or insomnia may occur rarely, but are usually mild and transitory. Other known possible side effects of the individual ingredients are: nausea, vomiting, diarrhea, rash, dizziness, fatigue, tightness of chest, abdominal pain, irritability, tachycardia, headache, and difficulty in urination.

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writers venture an opinion as to whether the psychological changes seen are the cause or the result of the illness. This is why it would be helpful to have a study comparing the findings in allergy with those in another chronic illness. Most allergists feel that one would be hard-pressed to describe a typical allergic personality; several well-constructed studies have indicated that there probably is not a typical personality either in the affected individual or in his mother.

In a comprehensive article that appeared in 1964, Freeman et al.¹ reviewed the majority of the related work that has appeared since 1950. They emphasize the findings that have been supported and point out the need for well-controlled experiments designed to uncover the relationships between psychology and allergy. Of most pertinence to the clinician is the fact that three of four recent studies have demonstrated psychological differences between groups varying in the extent of definite allergy as confirmed by skin and other provocative diag-

nostic procedures. There was an inverse relationship between the amount of true allergy present and the severity of the psychological disturbance. These findings would explain many of the discrepancies found among previous studies, because many of the groups of supposed allergic patients were in fact heterogeneous samples composed of those with and without significant immunologic sensitivity.

Freeman points out that though recent studies with the more carefully constructed groups are promising, confirmatory and more extensive studies are needed. However, in light of what has been done it behooves the clinician who may see patients with such illnesses as asthma, rhinitis, urticaria or eczema to carefully consider the role of true atopy in the production of a given individual's respiratory or dermatologic symptoms before saying the complaints are due to his "nerves".

S. Scott Nicholas, M.D.
Minneapolis, Minnesota

Reference

1. Freeman, E. H., Feingold, B. F., Schlesinger, K. and Gorman, F. J. Psychological Variables in Allergic Disorders: A Review. *Psychosom Med* 26:543, 1964.

Conservative Use of Thyroid Hormone*

I APPLAUD Dr. Olin's plea for conservatism in prescribing thyroid hormone. It sometimes seems to many endocrinologists that most patients who need thyroid hormone do not receive it and most who receive it do not need it. While this may not really be so, physicians are urged to exercise good clinical judgment in the administration of thyroid. If given in small or moderate dosage, these hormones may be harmless as placebo therapy, but it is neither "good medicine" nor intellectually satisfying to the physician for him to give thyroid indiscriminately.

When it has been decided that a given patient should be treated with thyroid substance, the physician should remember the effect the various thyroid hormone preparations have on thyroid function tests. He should remember that many patients who are

euthyroid while on treatment with l-thyroxine will have a higher-than-normal protein-bound iodine (PBI) value, all patients who are euthyroid on treatment with l-triiodothyronine will have a lower-than-normal PBI, and many patients who are euthyroid on treatment with desiccated thyroid or thyroglobulin will have a lower-than-normal PBI if the preparation used contains a significant amount of l-triiodothyronine; the thyroidal uptake of radioiodine (¹³¹I) by most of the patients treated with any of these substances will be markedly suppressed. If these facts are kept in mind, one will not fall into the trap of incorrectly changing the dose of thyroid hormone because of abnormal values of PBI or ¹³¹I uptake produced by the administered hormone itself.

Dr. Olin is rightly skeptical of the syndrome of "metabolic insufficiency." Many

Continued

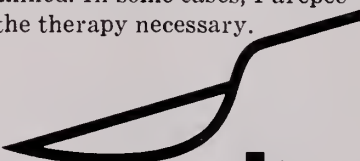
*See Olin, Ronald: The Use and Abuse of Thyroid Hormone. *Minnesota Med* 49:1233, 1966.



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endocrinologists are not sure that this syndrome actually exists. Certainly it is a very rare condition, and the vast majority of patients in whom this diagnosis has been made have psychoneurosis but no thyroid disorder.

In his article Dr. Olin mentions the use of thyroid hormone for the treatment of the ophthalmopathy of Graves' disease. With the discovery of long-acting thyroid stimulator (LATS), formerly held concepts of the

cause and treatment of this ophthalmopathy are being seriously challenged. Thyroid hormone seems to have little place in such treatment except for the correction of myxedema in those patients who have become hypothyroid as a result of ablation of the thyroid.

I hope physicians in general will adopt Dr. Olin's conservative attitude toward the therapeutic use of thyroid hormone.

William M. McConahey, M.D.
Rochester, Minnesota

Alcoholism and the General Practitioner

WE HAVE on our hands an insidious problem of massively endemic character and epidemic proportions: alcohol addiction. To the three leading causes of death — accident, cardiovascular disease, and cancer — there are three major contributing factors: each representing an addictive problem, namely: alcoholism, obesity, and tobacco.

Alcoholism is no longer a punitive but rather a socio-medical problem. Since 1935 thousands of alcoholics have demonstrated that they are neither helpless nor hopeless; through Alcoholics Anonymous they have arrested their illness. Not all, however, have been so fortunate. We are in error if we expect every alcoholic to be able to free himself from his addiction thru AA without the ancillary or primary support of other disciplines, including the medical profession.

Therefore it is unrealistic and futile for us to merely advise the alcoholic to stop drinking. He would if he could; but he can't. We must repudiate all this cavalier nonsense that the alcoholic lacks motivation, that he must sink to the bottom of the barrel or into the gutter before he can rise again, that he should humble himself on his knees and implore help.

To tell a spouse that the alcoholic husband or wife is not ready to stop drinking is tantamount to telling a patient with early cancer to return the following year when the tumor is larger and more invasive. We must intervene before the development of such figurative metastases as family aliena-

tion, job loss, and irreversible personality deterioration.

Shifting blame or rationalizing motives is a normal defense built on fear, for the alcoholic is afraid of life and knows that admitting his problem will mean surrendering the crutch he has a need to keep and use.

Like all other addictions, alcoholism is an escape mechanism and a comfort-seeking syndrome. As Kahlil Gibran, the Lebanese poet, has expressed it: "Comfort is a stealthy thing that enters the house as a guest, then becomes a host, and then a master." Since the alcoholic is not particular what agent he uses to secure his objective, there is always danger of a transference addiction involving the use of tranquilizers, barbiturates, amphetamines, or other drugs that can be just as destructive as alcohol.

Though becoming an alcoholic may be understandable, remaining one is neither understandable nor defensible with present interdisciplinary help available.

At Willmar the overwhelming proportion of patients who are psychologically evaluated have clear neurotic profiles. Psychoneurosis in its various manifestations, of which addiction is but one, is recognized as a treatable type of emotional illness. Though approximately 20 percent of alcoholics admitted to Willmar State Hospital cannot be rehabilitated because of chronic brain disease or

Continued

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character disorders and sociopathy which render them unamenable to group or individual counseling, 60 per cent of the remainder who receive treatment at our Willmar institution can be rehabilitated by concerted multidisciplinary effort.

While the medical profession must comprise the first echelon in the crusade against alcoholism, sociologists, psychologists, pastors, and others dealing with human problems must also recognize and openly acknowledge their joint social and moral responsibility to revitalize the alcoholic by imbuing him with a love of life so com-

prising and irresistible that he will choose full dedication to it rather than escape from it.

Finally, for greater permanence in the control of alcoholism, it is ethically incumbent on the medical profession to assist in changing the social image of alcohol consumption within the United States. By precept and example we physicians must convey the idea that it is an individual's personal prerogative to abstain from alcohol. Just as it is socially acceptable to take a drink, it should be equally acceptable to decline one and yet be considered 'one of the crowd.'

Director, Alcohol and Drug Addiction Unit, Willmar State Hospital.

Donald H. Petersen, M.D.
Willmar, Minnesota

Congenital Hemolytic Anemia

ANALYSIS OF MANY cases of congenital hemolytic anemia has for a long time been a source of frustration to the hematologist. Not only did he find himself hard pressed to help his patient, but he was even denied that ultimate pleasure, the ability to make an exact diagnosis. It was, no doubt, during a period of extreme dyspepsia engendered by the study of such a patient, that the sonorous title, "Congenital Non-Spherocytic Hemolytic Anemia," was invented. Such a tribute to medical ignorance could not long stand alone, so that Selwyn and Dacie, on the basis of a difficult and mysterious "auto-hemolysis test," soon subdivided the group into Types I and II, and the confusion began compounding.

Fortunately, there has been an explosion of both interest and information in the field of red cell biochemistry in recent years; and, with these developments, the congenital hemolytic anemias have begun to yield their secrets. A number of enzyme deficiencies have been found which appear to explain many of these cases, and one would predict that eventually biochemical mechanisms for all such cases will be uncovered. The most common defect is glucose 6-phosphate dehydrogenase deficiency, a sex-linked abnormality which usually has overt manifestations only after exposure to oxidant drugs. That this is not always true is shown by the case

reported in this issue. Deficiency of this enzyme is most common in Negroes, but is also seen in certain Caucasian groups, such as Greeks, Sephardic Jews, and others.

It is important to make a diagnosis of glucose 6-phosphate dehydrogenase deficiency, since many of the problems of these patients are avoidable if they are not exposed to certain drugs or chemicals. Unfortunately, a simple and reliable test that would ferret out all patients in all situations has been hard to find. Heterozygous females, since their enzyme levels may approach normal, are difficult to diagnose. Similarly, patients with high reticulocyte counts may give misleading laboratory results since reticulocytes have high levels of enzyme. This latter problem is particularly vexing since it may make diagnosis impossible immediately after a period of acute hemolysis, which is, of course, just the time when one usually wishes to make a diagnosis. The quantitation of Heinz bodies, as described by Beutler, is difficult and frequently unreliable. A variety of screening tests, based upon the rate of methemoglobin reduction by red cells or the rate of reduction of various dyes by red cell hemolysates, have been described. One rather simple "spot test" is commercially available. Unfortu-

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1. Schleif, R.H.: J.A.P.H.A., 46: 179, 1957 *U.S. Pat. No. 3,062,714

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nately, all these tests are more or less cumbersome and at times inadequate. Jacob and Jandl¹ have just reported a test for glucose 6-phosphate dehydrogenase deficiency which they state is valid both in female heterozygotes and after acute hemolysis when reticulocyte levels are high. The test appears simple and within the capabilities of many clinical laboratories. Hopefully it will make detection of red cell glucose 6-phosphate dehydrogenase deficiency levels more widely and reliably obtainable.

Whatever the test employed, however, efforts should be made to make a diagnosis of the exact enzyme deficiency in any case of congenital hemolytic anemia. It is now possible to prevent most clinical problems in the largest group of these cases; and eventually, as understanding of red cell metabolism increases, even specific therapy may become available.

F. Bruce Lewis, M.D.
Director of Medicine
Mount Sinai Hospital
Minneapolis, Minnesota

Reference

1. Jacob, H. S., and Jandl, J. H.: A Simple Visual Screening Test for Glucose-6-Phosphate Dehydrogenase Deficiency Employing Ascorbate and Cyanide. *New Engl J Med* 274:1162, 1966.

Urine Collection for Microbiologic Study in Females*

SINCE THE cornerstone of diagnosis and treatment of infection of the urinary tract is the identification of significant bacteria in the urine, it is essential to consider the techniques of collection of adequate specimens of urine for microbiologic study. Certainly, infection of the urinary tract is the commonest problem in the field of renal disease.

The procedures used to obtain a representative sample of urine must overcome the hazard of contamination. This is much more difficult in females than in males because of the genital anatomy and the possibility of contamination of the specimen by vaginal flora. Currently, three techniques are available for collection of urine for microbiologic study. These include catheterization, the midstream clean-voided collection, and needle aspiration of the bladder.

Catheterization does not eliminate entirely the problem of contamination since the catheter must pass through the urethra and can carry contaminants with it. Also a small but definite risk exists that the catheter itself may carry infection. Therefore, it is rarely needed in obtaining specimens for culture.

Needle aspiration of the bladder appears

to eliminate the problem of contamination and has not been accompanied by recognized complications in our experience. However, the procedure must be performed by a physician; therefore its use is limited to specific situations where low colony counts may be significant or to female patients from whom an adequate clean voided specimen cannot be obtained.

An adequate specimen can be obtained from most ambulatory females by means of the midstream clean-voided method but, as in any specimens for culture, careful attention must be given to rapid transportation and bacteriologic study using adequate quantitative techniques. Among ambulatory female patients seen at the Mayo Clinic, intermediate bacterial colony counts of less than 100,000 are being found in only approximately 7.5% of the specimens collected by this technique. With a repeat urine culture this percentage of possible contamination can be reduced even further, but we are also aware that colony counts of less than 100,000 can occur primarily in patients who have chronic infection secondary to anatomic abnormalities in the urinary tract, such as nephrolithiasis.

The midstream clean-voided technique becomes virtually worthless when left to personnel who do not understand the pro-

Continued

*Breitenbucher, B. R.: A Study of 425 Voided Urine Cultures in Women. *Minnesota Med* 49:1381, 1966.

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cedure. Close supervision is required, preferably by designated personnel specially trained in the procedure. In most situations the patient cannot be left to collect her own specimen, but must be assisted by a nurse using proper precautions and techniques. When this procedure is followed, adequate specimens can be obtained for appropriate diagnosis and subsequent treatment.

Hospitalized patients present a more difficult problem, since it is often impossible to collect an adequate specimen from a female in bed by either midstream clean-voided or catheterization techniques. When a specimen is required from patients in this situation, we often rely on the bladder aspiration technique.

Lynwood H. Smith, M.D.
Rochester, Minnesota

Addiction*

IT IS HEARTWARMING to see more articles that depict the problems encountered on a psychiatric service in a general hospital setting.

Although specific topics are relevant and pertinent, of more importance is the awakening realization, although belated, that the general community hospital is a focal "melting pot" of psychosocial problems. The reactions to tension, fear, rage, hate, and the need for love are becoming acceptable vectors** of disease. Society is demanding a new assessment — a psychologic "vivo," not

"vitro," study. People must come to accept their basic responsibilities to one another and the part they play in contributing to the "disease" state.

The general hospital setting can become a cohesive force in this direction by applying the total patient care concept rather than following the former system of considering solely the physical status of the individual. The crossroads are being reached; the community hospital is one way of seeking a final common path. Let us assist in its fruition and expansion.

Richard M. Steinhilber, M.D.
Rochester, Minnesota

*See page 189.

**See Test Your Word Score below.

Test Your Word Score

Vater — *Abraham Vater, German Anatomist 1684-1751 (page 169).*

Kocher maneuver — *cutting duodeno-parietal peritoneum to release duodenum (page 171).*

Stertorous — *snoring (page 177).*

Areflexic — *characterized by absent reflexes (page 179).*

Demographic data — *statistical study of population as pertains to health (page 191).*

Apogee — *highest point (page 195).*

Vasa vasorum — *small nutrient arteries and veins in the walls on the larger blood vessels (page 204).*

Vectors — *carriers of disease (see above editorial)*

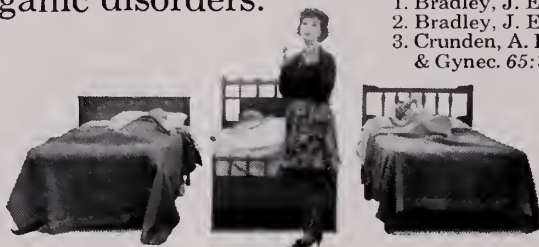
Anergy — *diminished sensitivity to specific antigens (page 250).*



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1. Bradley, J. E., *et al.*: J. Pediat. 38:41 (Jan.) 1951.
2. Bradley, J. E.: Mod. Med. 20:71 (Oct. 15) 1952.
3. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. 65:311 (Feb.) 1953.



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The Editor's Soliloquy

I Almost Broke My Arm

In looking over some of the correspondence in my files in order to eliminate some of its bulk, it was gratifying to reread some of the comments of satisfied readers:

"This week I have had a quiet day at home in which I could go through a lot of accumulated material, including copies of MINNESOTA MEDICINE — which has steadily improved under your editorship until it is now genuinely outstanding.

"Please extend my congratulations and appreciation to whoever did the condensing of my paper. He had it down to half its original length without sacrificing any important detail, thereby improving its readability and overall effectiveness."

Walter H. Judd, M.D.

"Thanks again for sending the copy to Dr. Roland Schoen, *Editor of ARIZONA MEDICAL JOURNAL*. I appreciate very much your helping my good friend."

Haddon Carryer, M.D.

Mayo Clinic

"Thank you for your note — I also appreciate the opportunity to express these thoughts in our fine state medical journal."

Colin B. Holman, M.D.

"It is so nice to have a thank you from the editor of the journal. I want you to know that my colleagues and I appreciate it."

R. K. Winkelman, M.D.

"I enjoyed very much the March issue of MINNESOTA MEDICINE. If I could obtain your permission, I would like to reproduce . . . In my opinion this piece of work is one of the classics we have run across from time to time."

H. Ellis Saxton, Exec. Editor
Industrial Medicine and Surgery

"I have just seen the issue. I think it is beautiful. You are to be congratulated. Your arrangement of these various rough diamonds has produced a memorable issue. I am delighted with the whole thing. Please let your colleagues on the editorial board know how much I appreciate the issue and the collaboration that has gone into it."

Raymond C. Read, M.D.
Wayne State University

"We are planning to use your editorial . . . in a forthcoming issue of *The New Physician*."

Mary Ruth Bonnell, Editorial Dept.

"This is just a note to thank you for your thoughtfulness in writing as you did about my knee injury. I am sure that my speedy recovery can be attributed equally as much to the heartwarming messages as to the expert medical attention."

Richard Nixon

"Thank you very much for your thoughtfulness in sending me a copy of the May issue of MINNESOTA MEDICINE, which contained a quotation used by my mother. I was indeed happy to read it."

Dwight D. Eisenhower

"May I thank you for sending the February issue of MINNESOTA MEDICINE. Your journal is beautifully done and I am proud to have my editorial published in it."

Raymond D. Pruitt, M.D.

"It was nice to meet you when you were here for the meeting of the American Medical Writers Association. You have done wonders with MINNESOTA MEDICINE."

Morris Fishbein, M.D.

"Congratulations on your splendid and perceptive Editor's Soliloquy 'The Physician's Gethsemane.' I am going to keep it and, if I may, I will probably quote from it from time to time. — Finally, congratulations again on the high quality of MINNESOTA MEDICINE. It is always a pleasure to read it."

Harold S. Diehl, M.D.

"Many thanks for the editorial in MINNESOTA MEDICINE. Despite our human shortcomings, ours is a great profession and playing a small role in its constant growth and progress is so satisfying. Many thanks for your continued support."

Edward R. Annis, M.D.

"I take the liberty of forwarding to you a copy of the sermon I delivered before members of the American Medical Association — it was a privilege for us to have the opportunity to be host to members of the AMA — with cordial good wishes."

C. Julian Bartlett, D.D., San Francisco

Continued

EDITOR'S SOLILOQUY

"May I once more write that MINNESOTA MEDICINE is truly blooming. There has been a continuous improvement to the point where the journal has all sails to the wind. Congratulations to you and the truly functioning board of editors."

Arthur H. Wells, M.D.

"The national recognition recently conferred . . . is but a reflection of the quality of its editorial board and the dedicated services which a dynamic editor contributes to this literary effort. A host of your professional colleagues join in this accolade."

Thomas P. Cook

"My compliments to you on the excellent edition of MINNESOTA MEDICINE. It certainly ranks as one of the outstanding state medical journals. You are to be congratulated."

Allan P. Thal, M.D.

University of Kansas

"For some time it has been on my mind to write to you and the board of editors to express my sincere appreciation—the publication itself is beautifully done. I can quite understand the recognition for excellence which has come to the journal under your direction."

John L. McKelvey, M.D.

"MINNESOTA MEDICINE has reached its all time high as a most outstanding medical journal. You and the hard working members of the board cannot be given enough credit for this achievement."

Harold W. Brunn

"Dr. Lester King, one of the editors of JAMA, spoke of a course on medical writing—and asked me if you would be good enough to send him 20 copies of one issue of MINNESOTA MEDICINE so it can be utilized in the teaching program. He felt that MINNESOTA MEDICINE was perhaps the best state medical journal."

Albert Sullivan, Jr., M.D.

University of Minnesota

"With a few extra thousand dollars, — I should think that MINNESOTA MEDICINE would be financially secure, a better journal, and a true competitor of the NEW ENGLAND JOURNAL."

W. J. Martin, M.D., Mayo Clinic

"Mr. Speaker, I would like to insert a very interesting article in the Congressional Record . . . which was referred to me by a very close friend and consultant, who has been very active in veterans affairs in my community. The article expressed in medical terms one of the major problems with which our nation is confronted — *The Gimmie Syndrome*, MINNESOTA MEDICINE 49:449, March 1966." Congressional Record, Oct. 18, 1966. Page 85370.

Hon. Joe T. Broyhill

Virginia, House of Representatives

"The publication itself is beautifully done, even for the layman. It is extremely readable and the circulation figures are impressive."

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"MINNESOTA MEDICINE exhibits good editing and I found much of interest—delighted to know that some doctors can write plainly and with a touch of humor."

Minneapolis Star-Tribune

George L. Peterson,

"Many thanks for your nice note. If you find my manuscript acceptable for publication in MINNESOTA MEDICINE, which has become a journal of distinction under your aegis and direction, I would like to believe that you would publish it all in one issue."

Owen H. Wangenstein, M.D.

It is to the diligent, hard-working, unselfish board members that all the credit is due. They write, they talk, and they coax manuscripts and editorials from overworked physicians wherever they can get them. They read, review, correct, stylize, edit, and re-edit unstintingly until manuscripts are about ready to come out of their ears. They forego their lunch, their coffee breaks, and their social hour in order to produce a good MINNESOTA MEDICINE. Pat yourself on the back for having such dedicated board members. It was for them that I almost broke my arm.

Carl O. Rice, M.D.

Old Doc Hess says: That woman married him for his money but she had to wait 40 years for it.

Our Senior Educators



Burtrum C. Schiele, M.D.

DR. SCHIELE'S EARLY memories emphasize Pike's Peak. He lived in Colorado Springs and went to Colorado College there for his bachelor of arts. His doctor of medicine took him to Colorado University at Denver, and he began his travels, which have grown steadily wider in scope, by taking an internship at Ancker Hospital in St. Paul. After a two-year fellowship as a Commonwealth Fund Fellow in psychiatry with Franklin Ebaugh at Colorado Psychopathic Hospital, he became assistant resident and then resident psychiatrist at Payne Whitney Psychiatric Clinic, New York. From there he went to the University of Minnesota where he has continued and is now chiefly doing research in psychopharmacology.

The Colorado mountain club's young Burtrum Schiele was the only son of a mining consultant. Whatever physical exuberance may have led him to climbing mountains, it appeared to weaken rather early in favor of wrestling with biological science. As an undergraduate, torn

Continued

between chemistry and biology, his choice moved in the direction of biology, possibly conditioned a bit by his being offered a job as student assistant in the biology department. Chemistry came to be represented at a rather low level by summer jobs at a filling station; but biology actually provided a student day's earning potential. Curiously predictive of an aspect of his much later work, he earned money for medical school expenses by collecting pollen for pharmaceutical houses. Most people collect Colorado cockle burrs with relative ease; in contrast, however, the pollen of the Colorado cockle burr is difficult to get, and among the first innovative efforts that appeared in Dr. Schiele's career was his development of new cockle burr pollen collecting methods. There was yet another early indicator of his later career when he received the first prize given by the college of medicine for achievement in clinical pathology. This prize was known as the Todd Prize, the donor being a relative of Minnesota's Todd, benefactor of the Todd Memorial Hospital, a part of the University of Minnesota Hospitals.

Later, graduating from a part-time job as desk clerk at the Colorado Psychopathic Hospital where he met the psychiatrist, Franklin Ebaugh, Dr. Schiele became the first of the Psychopathic Hospital's junior interns. Feeling a need to broaden his experience, he chose to leave Colorado to take his internship at Ancker Hospital in St. Paul. As is not uncommon, the internship experience established a relationship with one of the most attractive among Ancker's nurses, and the German strain in the Schiele family later became allied with a Scandinavian Pederson family when he married Evelyn Pederson. The Schieles have three children: two girls, and one boy. Gretchen, the elder daughter, established the Schieles as world travelers by an early interest in languages and in foreign service, spending some time in Europe where the family visited her. Ultimately she married a career state department man, and the young couple are now living in Laos. The Schieles expect to go there very soon, combining professional errands with 'round the world' travel and a visit to the young folks.

After internship Dr. Schiele returned to Colorado Psychopathic Hospital with Ebaugh for a two year residency in psychiatry. Ebaugh, who was at that time exceedingly active in American psychiatry, had been a student of Adolf Meyer, whose psychobiological orientation was particularly attractive to Schiele. Ebaugh was noted for his ability to push young scientists along, and after the two-year residency he was encouraging Schiele to leave Colorado again for further training and maturity. Ebaugh was so much a man to push his protégés along that he gave young Dr. Schiele and nurse Pederson a wedding present more than a year before they were married. In fact, typical of those times, the young pair that had met at Ancker were not finally married until they had been separated by a whole continent when Evelyn was a psychiatric nurse at Stanford University Hospital and Burt was a resident in New York with Diethelm.

Oskar Diethelm, also one of Adolf Meyer's students, represented further strong personal influence in the direction of biopsychology. Schiele continued for three years at Cornell Medical School with Diethelm and then came to the University of Minnesota in 1937 as assistant professor of psychiatry and neurology.

Dr. J. C. McKinley, who had been particularly interested and proficient in neurology, was then head of Minnesota's Division of Neuropsychiatry, at that time in the Department of Medicine. The Psychopathic Hospital had recently been established, and there was a real need for greater emphasis upon the psychiatric aspects of illness. During the earlier years at Minnesota, while Dr. Schiele continued to develop his neurological skills so that he obtained his National Board certification in both psychiatry and neurology, he nevertheless maintained the emphasis on psychiatry as his distinctive contribution during this whole period of his life. He was particularly interested in adult inpatient psychiatry and began to accept prime responsibility for this service in 1944, continuing his interest and activity until 1961 when he became principal investigator in a U. S. Public Health Service grant establishing a research unit in clinical psychopharmacology.

Dr. Schiele was one of the first psychiatrists in this region to begin clinical studies of the therapeutic effects of chlorpromazine, as reports of this drug appeared in the journals. Intrigued by his work in the area, Schiele took a quarter leave from University responsibilities to return to student status. He intensively reviewed his training in physiological chemistry and became familiar with modern structural chemistry. As a direct outgrowth of this growing interest he became, in cooperation with psychologist Gordon Heistad who is also interested and active in the behavioral correlates of pharmacological agents, the director of one of the first research units for early clinical drug evaluation sponsored by the National Institute of Mental Health. These units, as the name implies, were established to provide for early scientific evaluation of drugs before their release on the market. This new field increased so rapidly in national importance that another very long word was soon added to our vocabulary by establishment of the American College of Neuropsychopharmacology. Dr. Schiele is a charter fellow in this now well-established group.

Since 1964 Dr. Schiele has been a member of the Clinical Drug Evaluation Committee of the National Institute of Mental Health. In connection with that committee as well as in related fields, he has been much in demand for site visits in this country and abroad. His pioneering role in the clinical drug evaluation area makes his estimate of projects and settings unusually valuable. His previous experience and special training make him particularly respected among his peers because his talks and evaluations are full of information that is of direct interest and value to the practicing physician. In relationship to the research area he is particularly noted on the one hand for his emphasis on the dangers of artificial and over-controlled laboratory research unrelated to clinical application and, on the other hand, for his advocacy of carefully controlled practical studies in contrast to loose clinical evaluations.

With all his national and international activities Dr. Schiele has not neglected to fill an important role in local teaching and lecturing as well as in the encouragement of Minnesota research. He has long been a consultant to the St. Cloud Veterans Hospital; he serves on the State Medical Advisory Committee; he has established research bases in several state hospitals; and he organizes a steady flow of research within the

Continued

Psychopathic Hospital of the University. He is past president of the Minnesota Society of Neurological Sciences and of the Minnesota Psychiatric Society and has also found time for more routine committee service in Medical Sciences.

The following short bibliographic list provides a summary sample of the clinically oriented contributions that have appeared from the work of Schiele and his associates:

In conclusion I cannot forego a personal note. We all know that, however significant a man's scientific contributions may be, his role as a colleague and member of our community relates significantly to his professional achievements. I have been a neighbor and staff associate with Burt for nearly thirty years. This association has served to establish an invariable record of integrity and loyalty in the interpersonal life in which we have been participants. For most of us it is trite and in some way embarrassing to enumerate examples and to marshall adjectives when we wish to particularize the virtues of our friends. However, I am confident that those who are also privileged to know and appreciate these qualities in Burt and "Pedey" can easily supply the merited words of praise. I can only add my warm endorsement from long and intimate association.

Starke R. Hathaway, Ph.D.
Minneapolis, Minnesota

**Oliver Wendel Holmes, M.D.
To the Young Practitioner**

Ask the wisest practising physician you know, what branches of science help him habitually, and what amount of knowledge relating to each branch he requires for his professional duties. He will tell you that scientific training has a value independent of all the special knowledge acquired. He will tell you that many facts are explained by studying them in the wider range of related facts to which they belong. He will gratefully recognize that the anatomist has furnished him with indispensable data, that the physiologist has sometimes put him on the track of new modes of treatment, that the chemist has isolated the active principles of his medicines, has taught him how to combine them, has from time to time offered him new remedial agencies, and so of others of his allies.

But he will also tell you, if I am not mistaken, that his own branch of knowledge is so extensive and so perplexing that he must accept most of his facts ready made at their hands. He will own to you that in the struggle for life which goes on day and night in our thoughts as in the outside world of nature, much that he learned under the name of science has died out, and that simple homely experience has largely taken the place of that scholastic knowledge to which he and perhaps some of his instructors once attached a paramount importance.

Where to Look

Mitral stenosis may be concealed under a quarter of a dollar. It is the most difficult of all heart diseases to diagnose. — Osler



Curbstone Consultation

Ligation of Hepatic Artery

QUESTION: I have heard conflicting statements as to the mortality associated with ligation of the hepatic artery in humans. How serious actually is this injury when it occurs accidentally in patients with normal livers?

ANSWER: At one time it was felt that the mortality associated with accidental ligation of the hepatic artery would run about 60%. Such figures were based on observations made in the pre-antibiotic period and included all cases of hepatic artery ligation. On retrospectively reviewing many of the cases on which such a mortality figure was based it is now apparent that death was undoubtedly due in many instances to causes unrelated to the arterial ligation.

More recent observations would indicate that ligation of the hepatic artery or one of its branches is not ordinarily fatal in an otherwise uncomplicated case. When this injury does occur, however, attention must be given to preventing deleterious influences from secondary factors, such as shock and sepsis. Such added factors could diminish the collateral flow or increase the hepatic oxygen need, thereby leading to unfavorable consequences.

Harold D. Kletschka, M.D.
Syracuse, New York

Sarcoidosis

*QUESTION: Is the presence of fever of prognostic significance in a patient with sarcoidosis?**

ANSWER: Perhaps forty per cent of patients with sarcoidosis will have fever attributable to the disease. Negroes have a higher incidence than white patients. Although fever generally may not be thought of as a significant feature of sarcoidosis, in one study thirty-two per cent of such patients exhibited a temperature elevation between 101° to 103° and ten per cent had temperature elevations above 103° F. The occurrence of fever is not dependent on the extent or localization of the disease although erythema nodosum is more common among febrile patients. The pathogenesis of the fever in sarcoidosis is unknown. It is unreliable to prognosticate on the basis of an associated fever. Although hospitalization may be more prolonged in febrile cases this difference may be attributable to delay in diagnosis because of inability to appreciate the association of fever with sarcoidosis.

Harold D. Kletschka, M. D.
Syracuse, New York

*See Minnesota Med 47:19, 1964.

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The Viewing Box

Chest Pain with Negative Chest Roentgenogram

A 35-year-old white female entered the Outpatient Department of the St. Paul-Ramsey Hospital complaining of nervousness and anxiety. She also complained of a single episode of shortness of breath without chest pain. There was no history of expectoration, hemoptysis or hoarseness, but she had previously noted some dysphagia. She had been delivered of a normal pregnancy one month previously and following this had been placed on a mild tranquilizing agent and "birth control pills." Examination disclosed some questionable diminution of breath sounds in the right lower lobe area; otherwise no abnormal physical or laboratory findings were present. After one hour she was discharged from the Outpatient Department.

Three days later she was admitted to the hospital complaining of chest pain. Again physical examination was negative except for a pulse rate of 108 per minute. The chest x-ray was considered negative (Figure 1). She was placed on strict bed rest and heparinized. Against orders she got up to go to the bathroom and became dyspneic and cyanotic and collapsed. No blood pressure reading could be obtained, and her pulse was very weak and fast. Her blood pressure was artificially elevated and a chest roentgenogram plus a lung scan using I^{131} tagged macro-aggregated serum albumen was obtained.

What is your diagnosis? (See next page.)



Figure 1

DIAGNOSIS: Pulmonary embolism.

The interpretation of the lung scan indicated multiple areas of pulmonary embolism of the right upper and lower lobes and totally of the left lower lobe (Figure 2). An immediate catheterization of the right side of the heart was done and a pulmonary angiogram obtained. The pulmonary artery to the left lower lobe was completely occluded (arrow, Figure 3). Comparison with the admission chest film disclosed a cut-off of the arterial supply to the left lower lobe on that film (Figure 1 and arrow, Figure 2). Following digitalization she had an immediate plication of the inferior vena cava.



Figure 2



Figure 4



Figure 3

Followup chest roentgenogram and lung scan (Figure 4) after one week showed improvement in lung vascularization and some resolution of the infarcted areas. (Lung scans are superimposed on the admission chest film for comparative purposes.)

She was discharged on a regimen of Coumadin.

M. R. Gilchrist, M.D.*

C. W. Frye, M.D.*

St. Paul-Ramsey Hospital

*Department of Radiology

References

1. Ormond, R. S., Gale, H. H., Ellet, H. D., Gahogan, T.: Pulmonary Angiography and Pulmonary Embolism. *Radiology* 86:658, 1966.
2. Loken, M. K. and Bugby, R. D.: Visualization of the Lung by Methods of Scintigraphy. *Amer J Roentgen* 97:850, 1966.

Medical Seminar

Hereditary Hemorrhagic Telangiectasia

Rendu-Osler-Weber Syndrome

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THE SYNDROME of hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease) is characterized by the triad of multiple telangiectases, hemorrhage, and a familial history. The telangiectases with or without hemorrhage can involve almost any organ. Although not very common, the disease must be considered in the differential diagnosis of unexplained bleeding from any body organ. Epistaxis is the most frequent bleeding problem.

It is not known who first wrote of this disease. Babington,¹ and Legg,² both in the last half of the 19th century, noted the familial occurrence of epistaxis. A number of Legg's patients had cutaneous lesions, and perhaps a few of them were afflicted with hereditary hemorrhagic telangiectasia. Rendu³ recognized the association between epistaxis and multiple angiomas or telangiectases when he presented a case in Paris in 1896, the familial character of which was appreciated by Rendu, as his patient's mother, father, and brother had repeated hemorrhages. Both Rendu³ and Legg² considered the familial bleeding to be atypical hemophilia or pseudohemophilia. Osler⁴ established this syndrome as a clinical entity by separating it from the large and confused group of hemorrhagic diseases, and he documented the clinical features in a manner that remains a classic. Weber⁵ elaborated on the clinical and genetic features of the disease; but it was Hanes,⁶ in 1909, who de-

tailed the histopathology of the lesions and proposed the name hereditary hemorrhagic telangiectasia. Hanes has been called the forgotten man in what has come to be known as Rendu-Osler-Weber disease. Weber's⁷ later work, in 1924, called attention to the clinical spectrum of the disease that ranges from familial epistaxis to the full-blown syndrome of familial epistaxis with widespread telangiectases. He also included familial hematuria, familial gastrostaxis, and familial hemorrhoids as manifestations of the same developmental defect.⁸

Goldstein^{8,9} reviewed reports in the literature up to 1931 of the estimated 90 to 95 families with 500 to 550 members who had the disease. He emphasized that bleeding from most organs, including the eye and brain, could be associated with telangiectasia. Epistaxis was noted to be the most common bleeding problem.

Clinical Features

The principal feature of the disease is hemorrhage from telangiectatic lesions of the affected organ. Epistaxis is the most frequent symptom, and although epistaxis can occur in infancy, it usually begins in childhood.¹⁰ A decrease in frequency of nosebleeds or even a remission of all symptoms during adolescence or pregnancy has been observed.^{10,11}

The cheek, lips, mouth, tongue, nasal sep-

Continued

tum, inferior turbinates, and fingers are the most apparent sites of the telangiectases. Lesions also may be found on the trunk and hands and beneath the fingernails. During childhood and adolescence, the telangiectases are obscure or absent; they tend to become more prominent and increase in number between the ages of 35 and 50 years. The skin is involved in all but a very few patients with hereditary hemorrhagic telangiectasia. It may be necessary to scan the entire epidermis very carefully in some patients or family members to find one or two tiny lesions. The telangiectatic blemishes, however, are usually obvious. Serious hemorrhage from the skin is rarely a problem because of accessibility of the lesions and the protective layer of stratified squamous epithelium.

Most of the patients come to the physician because of epistaxis. Some patients with nosebleeds probably are treated without the underlying disease being recognized. Bleeding often occurs daily and can be triggered by a cough, sneeze, or slight trauma. At times, epistaxis begins while the patient is lying quietly or even sleeping. Saunders¹² described one patient who required more than 2,000 blood transfusions, and death from epistaxis has been reported.¹³ At the other extreme, the bleeding may be only a minor ooze that occurs at infrequent intervals and is easily managed by the patient himself.

Telangiectases of the anterior nasal septum, inferior turbinate, and floor of the nose are particularly vulnerable to slight trauma, with resultant hemorrhage. Patients often are seen with septal perforations from repeated packing or cautery.

The gastrointestinal tract is another common site of telangiectases. Gastrointestinal lesions may be present and bleed in individuals who do not have obvious cutaneous or oral lesions.^{14,15} The more frequent causes of gastrointestinal bleeding, for example, peptic ulcer, can coexist in patients with visceral, nasal, or cutaneous telangiectasia.

The association of pulmonary arteriovenous fistula in individuals with hereditary hemorrhagic telangiectasia is well documented. Hodgson and Kaye¹⁶ reported that

49% (17 of 35) of their patients with arteriovenous fistula had a family history of hemorrhagic telangiectasia and 66% (23 of 35) were found to have telangiectasia on examination. They advise alertness to the development of arteriovenous fistula in persons in a family with hemorrhagic telangiectasia and recommend that these individuals have periodic chest roentgenograms.

Other less common sites of lesions are the brain, urogenital tract, and eye. Bird and associates¹⁷ found that approximately 10% of patients with hereditary telangiectasia did not hemorrhage.

The telangiectases of the skin and mucous membranes take three forms: (1) tiny, pinpoint, purplish red spots most often found on the face and hands and easily overlooked; (2) flat spider forms, the most common lesions, which resemble crushed spiders and are cherry red and two to three mm. in diameter, and (3) large, nodular telangiectasia, the lesion seen in older patients in whom a nodule the size of a split pea arises from the center of a flat spider form. All three forms are nonpulsatile, blanch with pressure, and bleed in an arterial fashion when traumatized. Monroe and Spencer¹⁸ emphasized that children in affected families usually have small spider-type cutaneous lesions that can be difficult to find. Failure to recognize these early lesions probably accounts for the rare diagnosis of hemorrhagic telangiectasia in children in the first decade of life. This phenomenon of occult cutaneous lesions may also explain the so-called "skipped generations" or atavism postulated by Fitz-Hugh.¹⁹

Laboratory Findings

Hypochromic, microcytic anemia almost always occurs in patients with bleeding lesions. Hemoglobin levels of 4 gm. are commonly reported.¹³ Results of tests of the bleeding and coagulation mechanism are normal. Abnormal results of the tourniquet test have been reported, but it is probable that the tourniquet merely brings into prominence the very tiny telangiectases that were not previously noticed and which were misinterpreted as being petechiae.

Histopathologic Features

Under the microscope, dilated endothelial lined spaces can be seen. Hanes⁶ noted an absence of muscle and elastic tissue in the walls of the superficially dilated vessels. This observation, however, has been disputed by Bean.²⁰ In the skin, the endothelial spaces lie immediately beneath the epidermis; the papillary layer of the corium is thinned, and the stratum germinativum is absent. In the nose, the dilated endothelial spaces lie just beneath the pseudostratified columnar epithelium.

Heredity

The hereditary features of hemorrhagic telangiectasia have been thoroughly studied.^{8-10,17} The disease is transmitted as a Mendelian dominant gene, with complete penetrance and no sex predilection. A positive family history of repeated hemorrhage or skin lesions or both is found in most patients. Stecker and Lake¹¹ recorded a positive family history in 86% of their patients. The finding of the 14% who did not have a positive family history was explained by the fact that most relatives were asymptomatic and that the disease was not recognized. In a study of the 491 descendants of a polygamous Utah pioneer, Dolowitz¹⁰ traced the disease through six consecutive generations. A single case is recorded of a progeny of two parents with hemorrhagic telangiectasia by Snyder and Doan.²¹ The infant died within three months from bleeding of multiple organs including the skin. They postulated that the homozygous state is lethal.

Treatment

A review of the multitude of treatments proposed for hereditary hemorrhagic telangiectasia is a study of alternating enthusiasm and disappointment. In certain instances there appears to be no lasting method to stop the bleeding. Old lesions reappear after vigorous attempts to destroy them, or new ones appear in their place or nearby. Stecker and Lake¹¹ caution conservatism "... only enough treatment, that is, to control the symptoms within tolerable limits without attempting drastic therapy

which might possibly aggravate the symptoms."

Treatment has involved three basic approaches: (1) local therapy in an attempt to control the bleeding, (2) systemic medications in the hope of altering the susceptibility of the lesions to bleeding, and (3) treatment of the anemia that is invariably part of the disease.

Local Treatment

Epistaxis, the major clinical problem, has been managed in numerous ways. Mechanical packing with cotton, absorbable gelatin sponge (Gelfoam), gauze strips of petrolatum (Vaseline), and various balloon devices may provide temporary assistance. There probably is some merit to the patient's carrying a self-inflatable balloon device, which helps him achieve some peace of mind, knowing that he is not totally dependent on assistance from others when his nose bleeds. The use of packs soaked in Russell's viper or moccasin snake venom is of historic interest. The nasal chambers of a number of patients have undergone partial necrosis from such packs only to later develop bleeding sites beyond the damaged area. Electrocautery has its advocates,²² but even the most enthusiastic technicians admit the frustration of finding new lesions adjacent to the recently cauterized nasal membrane. Septal perforation is a common sequela to extensive electrocautery or chemical cautery. Other local methods tried without uniform success include direct nasal implants of radium; conventional irradiation; radioactive cobalt irradiation; surgical removal of the entire nasal septum; submucous resection; ligation of the external carotid, internal maxillary, and ethmoidal arteries; and turbinectomy.

The recent innovation of internasal skin grafting as advocated by Saunders^{12,23,24} and others^{11,25} is a promising contribution to the local management of the problem of epistaxis of this generalized disease. The principle of grafting is to substitute tough squamous epithelium for the more fragile respiratory epithelium on the vulnerable

Continued

areas of the anterior nasal passages. The original procedure of Saunders,²³ which involved grafting the anterior septum, has been expanded to the grafting of the anterior lateral wall, the floor of the nose, the upper lateral cartilage area, and even the entire septum. The results of the various grafting techniques are encouraging, but severe epistaxis has not always been stopped. Saunders¹² has observed that most of his patients bleed after dermatoplasty but that bleeding is generally much less than before. In contrast, Stecker and Lake¹¹ admit that the bleeding of two of their 12 patients was greater after grafting. They believed that the drying of the nose which follows skin grafting contributes to further bleeding from lesions posterior to the grafted area; these posterior lesions were not present or were not apparent at the time of dermatoplasty.

Patients with pulmonary arteriovenous fistula should have the lesions removed surgically, particularly if there are only one or two. The unoperated patient is subject to the complications of hemothorax, heart failure, and brain abscess.

Systemic Medications

A large number of systemic medications have been advocated in the management of hemorrhagic telangiectasia. Most of the drugs were directed to the control of the bleeding by lessening coagulation defects or improving vascular permeability: problems that in most cases do not exist. Vitamins K, P, and C, snake venom, rutin, and corticosteroids have all failed to decrease the troublesome epistaxis. Koch and associates²⁶ and Harrison^{27,28} have reported success with the use of orally administered estrogens in the management of epistaxis. Harrison has biopsied the nasal mucosa after prolonged administration of ethinyl estradiol and demonstrated that the usual nasal respiratory epithelium was replaced by stratified squamous epithelium. The desired result of a decrease in frequency and severity of the nosebleeds was obtained in all 20 patients within one to three weeks of estrogen treatment, but unfortunately there was a prompt

relapse after therapy was terminated. Epistaxis is the only form of hemorrhage that has been controlled by the administration of estrogens, but there are obvious drawbacks, particularly in the male, to prolonged estrogen therapy. Saunders²³ stated the belief that estrogens are best used only in patients that continue to bleed after dermatoplasty.

Treatment of the Anemia

The correction of anemia from blood loss by the use of orally administered iron and by transfusion remains an important part of the management of this disease.

The handling of the individual patient necessarily combines the various approaches as needed. Correction of the anemia, local lubrication of the nasal membranes to prevent drying as well as use of pledgets, packs, inflatable balloons, and electrocautery of single troublesome lesions should provide a tolerable existence for most patients. When epistaxis continues to be a difficult problem, split-thickness skin grafts to the anterior septum, anterior tips of the inferior turbinates, and floor of the nose are recommended. The judicious use of orally administered estrogen after grafting seems reasonable.

Prognosis

Hereditary hemorrhagic telangiectasia varies from completely asymptomatic individuals to those with diffuse telangiectases and repeated massive hemorrhage. In most cases, the condition lies between these extremes.

Spontaneous, complete remission of symptoms has been reported.¹¹ Two of the three remissions noted by Stecker and Lake¹¹ occurred during pregnancy and persisted after delivery. Hereditary hemorrhagic telangiectasia usually is compatible with life but at times offers a miserable existence. Death, when it does occur, is usually due to profound anemia or shock or to the hazards of repeated transfusion. Houser¹³ estimates a mortality rate of 4% directly attributable to the disease.

Summary

Hereditary hemorrhagic telangiectasia is

a well-defined clinical syndrome characterized by the triad of bleeding from multiple sites (particularly the nose), cutaneous or oral lesions, and a positive family history. The bleeding can be very trivial or incapacitating. The full clinical spectrum can be seen in the same family. Epistaxis is the most frequent bleeding problem.

Treatment should involve the least drastic

procedures necessary to control the symptoms. Iron replacement or transfusions are usually necessary. Orally administered estrogens probably have some value, particularly when they are given after nasal dermatoplasty in patients who continue to bleed from the nose. Single pulmonary arteriovenous fistulas are best resected to avoid complications.

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Lawrence W. DeSanto, M.D.*
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References

1. Babington, B. G.: Hereditary Epistaxis. *Lancet* 2:362, 1865.
2. Legg, Wickham: A Case of Haemophilia Complicated With Multiple Naevi. *Lancet* 2:856, 1876.
3. Rendu: Cited by Weber, F. P.⁵
4. Osler, William: On a Family Form of Recurring Epistaxis, Associated With Multiple Telangiectases of the Skin and Mucous Membranes. *Bull Johns Hopkins Hosp* 12:333, 1901.
5. Weber, F. P.: Multiple Hereditary Developmental Angiomata (Telangiectases) of the Skin and Mucous Membranes Associated With Recurring Haemorrhages. *Lancet* 2:160, 1907.
6. Hanes, F. M.: Multiple Hereditary Telangiectases Causing Hemorrhage (Hereditary Hemorrhagic Telangiectasia). *Bull Johns Hopkins Hosp* 20:63, 1909.
7. Weber, F. P.: Developmental Telangiectatic Hemorrhage and So-Called "Telangiectasia" — Familial and Non-familial. *Brit J Child Dis* 21:198, 1924.
8. Goldstein, H. I.: Hereditary Hemorrhagic Telangiectasia With Recurring (Familial) Hereditary Epistaxis: With a Report of Eleven Cases in One Family. *Arch Intern Med* 27:102, 1921.
9. Goldstein, H. I.: Goldstein's Heredofamilial Angiomatosis With Recurring Familial Hemorrhages (Rendu-Osler-Weber's Disease). *Arch Intern Med* 48:836, 1931.
10. Dolowitz, D. A.: Hereditary Hemorrhagic Telangiectasia. *Amer Surg* 19:776, 1953.
11. Stecker, R. H., and Lake, C. F.: Hereditary Hemorrhagic Telangiectasia: Review of 102 Cases and Presentation of an Innovation to Septodermoplasty. *Arch Otolaryng* 82:522, 1965.
12. Saunders, W. H.: Septal Dermoplasty: A New Operative Procedure for Control of Nosebleeds in Patients With Hereditary Haemorrhagic Telangiectasia. *J Laryng* 77:69, 1963.
13. Houser, K. M.: Hereditary Hemorrhagic Telangiectasia. *Ann Otol* 43:731, 1934.
14. Henry, G. A.: Hereditary Hemorrhagic Telangiectasis. *Laryngoscope* 63:823, 1953.
15. Amerson, J. R., and McGarity, W. C.: Massive Gastrointestinal Hemorrhage due to Hereditary Hemorrhagic Telangiectasia. *Amer Surg* 26:707, 1960.

16-28 May be secured from the author or the reprints.

Green Medicinals

Herbs for the Brain

Ecclesiasticus said: The Lord hath created medicines out of the earth and a wise man will not abhor them. For improving the brain and its potential, herbal repertories include such simples as amaranth, dill, ivy, lachnanthes, mugwort, rosemary, strumonium, and wormwood — with the following recipe for a savory rosemary sauce:

Rosemary Sauce

Into one and a half ounces of butter throw a very finely chopped sprig of rosemary and fry for one minute. Add an ounce of flour and mix it well in the butter. Then add a pint of stock, the juice of a lemon and a tablespoon of anchovy sauce. Boil well together for ten minutes.

— C. F. Leyel, Green Medicine



look, kid, I gotta know your birthdate

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Book Reviews

Something is learned every time a book is opened. — Chinese proverb

EARLY MANAGEMENT OF ACUTE TRAUMA —
Nahum, C. V. Mosby, Publication Date 7-12-66,
Price \$21.00.

This subject which is so important for young physicians to grasp at the earliest possible time in their practice is very difficult to cover with completeness in 326 pages. This text, which is the work of 21 different authors, suffers somewhat from its brevity, yet certain of the chapters are particularly good — notably that on genitourinary system injury.

The broad principles of trauma management are well delineated and the overall purpose of providing a practical medical background for those who are to care for the traumatized patient is achieved. The book, however, will be of most value to interns and residents.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

APPLIED HYPNOSIS AND POSITIVE SUGGESTION — G. A. Ulett and D. B. Peterson, C. V. Mosby Company, St. Louis, 1965. 134 pages, \$8.50.

This primer is written in an easy to read style with very little verbiage. It should be of interest to physicians, dentists and others of the healing arts team wanting to learn methods, limitations and difficulties of hypnosis, as well as for more casual reading for interest's sake. The format is comfortable, arranged with subtitles for the reader's benefit and ready grasp. Would that more topics were presented in this manner! Two transposed sentences will likely be correctly arranged in later printing.

The authors "look upon hypnosis as the useful extension of the doctor-patient relationship." Twenty per cent of patients can be hypnotized to the stage of trance. Ulett and Peterson consider phenomena short of this as hypnotic, since the borderline is not easily defined. They have broadened the definition of hypnosis by including the stronger aspects of response to suggestion. One gets the impression that so long as the desired symptom relief or behavioral modification is achieved, some element of hypnosis has occurred.

Their discussion of the use of enthusiasm and positive suggestion, positive statements and words rather than those with more negative connotations indicates an approach which physicians can use to better advantage. They label this as part of the art of medicine, which is true as long as it is used intuitively as in the past. Now that suggestion can

be used with awareness, understanding and replication, it could well be considered as part of the science of medicine.

Attention to the positive approach in the physician-patient relationship is in good order whether described in the hypnosis model, response-reward construct, interactional psychology, or some other approach. This has merit as an intrapsychic process as well.

The authors dispel the aura of "evil mysticism" and the "unknown" and fearsome danger often associated with hypnosis. They offer adequate precautions, such as a rule that each physician should stay within the limits of his training. For example, an obstetrician using hypnosis should not use it to treat psychosis in a patient.

They discuss the history, theories, and nature of hypnosis, its use for symptom removal, pain relief, recovery of the memory of forgotten incidents, analgesia and anesthesia. A variety of areas of use are described by chapter titles: the use of hypnosis in medicine, surgery, psychiatry, obstetrics, auto-hypnosis, hypnosis in habit control, and hypnosis in children. They present this as a means to an end and recognize the merit of adjunctive therapies. Other chapters deal with methods of inducing, deepening and terminating hypnosis, with emphasis on proper selection of patients based on adequate diagnostic considerations. They describe physical and verbal components of the process, the direct approach, and the methods of obfuscation. Interestingly, they talk of the "double blind" as if it were a common term. (A reference to Bateson, G., Jackson, D. D., Haley, J., Weakland, J. H.: "Toward a Theory of Schizophrenia," Behavioral Science, 1:251-264, 1956 should be included in the bibliography.)

The hypnotic process is a complementary interaction in which the physician seems to be in control. The authors maintain, however, that the physician is only making use of the patient's response patterns and that in actuality the patient is in control of what he does.

Their thesis throughout is supported by cogent, concise examples. Their enthusiasm and positive presentation is understandable, but perhaps a little over-selling. The reader needs be wary lest Ulett and Peterson cast a spell over him, under which he would feel impelled to practice hypnosis.

Titus P. Bellville, M.D.
Minneapolis, Minnesota

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Clinical Path Conference

Leuko-Erythroblastic Anemia in Gastric Carcinoma

Dr. Robert Strom:

Case Report

A 38-year-old white female had noted intermittent upper abdominal distress occurring between meals and relieved by milk and antacids for approximately two years. For five weeks epigastric distress had increased in severity and a constant, aching pain had developed in the left hip. A prepyloric gastric ulcer was demonstrated on the upper gastrointestinal series. Epigastric pain and persistent vomiting necessitated the patient's hospitalization. Multiple purpuric lesions of the skin were present on physical examination. The serum amylase was 68 Symogi units. Two units of whole blood were transfused.

The patient was transferred to Hennepin County General Hospital, because of the onset of progressive abdominal distension. There was a history of a ten-pound weight loss over the past month. Medications included aspirin compound, phenobarbital, Probanthine and Darvon Compound.

She presented as a young white female in moderate distress with multiple skin ecchymoses. Blood pressure 130/80, pulse 100/min., temperature 99.6° Fahrenheit, weight 134 pounds. Auscultation of the heart revealed a soft systolic ejection murmur. The lungs were clear to auscultation and percussion. The abdomen was slightly distended and hypertympanitic. Bowel sounds were absent, and there was a diffuse abdominal tenderness, particularly in the area of a midline scar.

Laboratory studies included a hemoglobin of 9.8 grams %, white blood cell count 3,700 per cubic millimeter with neutrophils 71%, lymphocytes 26% and eosinophils 3%. The hematocrit was 27% and the prothrombin time 19.8 seconds. The direct platelet count was 26,000. The bleeding time was greater than ten minutes and the clotting time 17 minutes. A direct and indirect Coombs' test were negative. The fibrinogen level was reported as normal. Blood electrolyte studies showed a serum sodium of 139 mEq/L. per liter, potassium 3.5 mEq/L. per liter, Co_2 28 mEq/L. per liter, and chlorides 94 mEq/L. per liter. Blood urea nitrogen was 11 mg. % and the blood sugar 113 mg. %. Examination of the peripheral blood smear revealed increased red blood cell polychromasia and occasional nucleated red blood cells. The plasma hemoglobin was negative. Serial stool guaiacs revealed no occult blood. Urinalysis showed a specific gravity of 1.015, pH 8, albumin trace, and no sugar. Microscopic examination of the urinary sediment revealed 150 red blood cells and 45 white blood cells per high power field. A flat plate of the abdomen showed multiple air-filled loops of bowel.

A barium enema failed to show evidence of colon obstruction. Several transfusions of whole blood and platelet-rich plasma were given on the first hospital day. Repeated transfusions were necessary to maintain the hemoglobin at a level of 10 grams %. An operation was performed on the second hospital day.

Continued



Fig. 1 — Upper gastrointestinal series of x-rays showing gastric ulcer indicated by arrow.

Discussion

Dr. Robert McAllister*:

I am happy to be here today to discuss what appears to be a straightforward case initially, but becomes somewhat more complicated as the protocol develops. It seems to me that early in the protocol the history is quite compatible with an ordinary gastric ulcer. This relatively young woman had a two-year history of abdominal pain, relieved by taking milk and antacids. Her initial hospitalization with intractable pain and vomiting appears to represent some type of gastric outlet obstruction. The patient was then admitted to this hospital after abdominal distension developed. The abdomen was silent and diffusely tender. An adynamic ileus could be associated with the abdominal tenderness and this does not necessarily mean that a peritonitis was present.

X-rays

Dr. Mario Pleigo:**

The initial roentgenogram of the chest taken at the outside hospital is essentially normal with no active pulmonary disease. Several minute radio-dense shadows are seen on the films of the pelvis, involving the ischia and upper femora. The nature of these densities is not clear but they could represent bone islands or osteoblastic metastases. The upper G.I. series shows a persistent collection of barium on the greater curvature of the stomach (Figure 1). There are multiple radiating folds from

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**Associate Radiologist, Department of Radiology, Hennepin County General Hospital.

this collection of barium and all other radiographic findings suggest a benign gastric ulcer. The abdominal flat plate reveals gas-filled loops of small and large bowel distributed throughout the abdomen. A diffuse ground-glass density is also seen throughout all the films. This suggests an adynamic ileus with a superimposed accumulation of ascitic fluid.

Dr. McAllister:

It is important to know at this point that the patient remained distended despite nasogastric suction. Bowel sounds were absent and later a barium enema showed no evidence of large bowel obstruction. These factors point toward a diagnosis of adynamic ileus rather than a mechanical bowel obstruction. As a cause of adynamic ileus we must consider hypokalemia secondary to vomiting. The serum potassium is at the lower level of normal; however, it may not be an accurate reflection of the total body potassium. Another possible etiology to be considered in view of her purpuric lesions and hematuria would be intraabdominal or retroperitoneal bleeding. Perforation of the gastric ulcer with chemical or bacterial peritonitis or associated pancreatitis may present with an adynamic ileus. The presence of necrotic bowel secondary to arterial or venous occlusion or due to a diffuse vasculitis might also be considered.

The predominant initial laboratory findings were anemia, thrombocytopenia and an abnormal prothrombin time. The bleeding time may be expected to be prolonged in the presence of thrombocytopenia. The blood smear showed minimal hypochromasia; however, since multiple blood transfusions were administered shortly after hospitalization this finding may have been altered. Do we have any idea about this patient's history of pregnancy?

Dr. Gerald Onstad*:

The patient had had three previous pregnancies and had delivered three normal infants without complication.

Dr. McAllister:

The anemia present on admission could represent chronic intermittent bleeding from the gastric ulcer or a mild iron-deficiency anemia due to her previous pregnancies. What is not compatible with a bleeding gastric ulcer, of course, is the thrombocytopenia, the elevated prothrombin time and purpura in the presence of guaiac negative stools.

Thrombocytopenia

Thrombocytopenia may be conveniently divided into the idiopathic variety or a secondary thrombocytopenia associated with a large group of miscellaneous factors, including chemical and physical agents which might depress the platelet count. Considering first the chemical agents, she certainly was exposed to a number of things that have been reported to be associated with thrombocytopenia. Salicylates or phenobarbital could cause thrombocytopenia on a hypersensitivity basis. There appears to be no evidence of physical agents or x-ray treatment which might have lowered the blood platelets. An idiosyncratic reaction secondary to salicylate ingestion could give this picture.

*Department Internal Medicine, Hennepin County General Hospital.

Continued

Another large category of diagnoses known to cause thrombocytopenic purpura are the various hematopoietic disorders, such as leukemia, aplastic anemia, or pernicious anemia. One of the hallmarks of vitamin B-12 or folic-acid deficiency is thrombocytopenia. Certain hemolytic anemias may also be associated with thrombocytopenia. We would not likely consider any splenomegalic disorders here since the spleen was not noted to be palpable. Thrombotic thrombocytopenic purpura would also have to be considered because of the anemia, low platelet count and purpura. Certain viral infections are also associated with thrombocytopenia.

Consumption Coagulopathy

With the prolonged prothrombin time we would have to think of any disease that might lower the coagulation factors 5, 7 and 10, prothrombin or fibrinogen. Since abnormalities in any one of these factors are reflected in the one-stage prothrombin time, the presence of hepatic disease might be suspected. An excess of a circulating anticoagulant could interfere with clotting parameters. Congenital deficiencies of factors 5, 10 or fibrinogen would certainly have been detected in the patient's family history. Liver disease alone may be associated with a prolonged prothrombin time. It would be important to know whether or not this patient had received any antibiotics in the recent past?

Dr. Onstad:

As far as we know the patient had received no antibiotic medication.

Dr. McAllister:

Antibiotic therapy is known to enhance a Vitamin-K deficiency; however, this seems to be excluded by the history. The administration of salicylates in the presence of liver disease, could well induce depression of the clotting factors. A penetrating posterior gastric ulcer leading to a pancreatitis might liberate coagulation factors, particularly thrombin, into the blood stream and cause the clotting mechanism to be accelerated. In most instances the clotting factors would be used up because of diffuse intravascular coagulation, primarily effecting the small blood vessels. The normal amylase observed is against pancreatitis, but does not exclude that diagnosis. The normal fibrinogen level also makes a consumption coagulopathy a more remote possibility.

Collagen Diseases

My initial impression on reviewing the protocol was that of a collagen disease with thrombocytopenia and later pancytopenia associated with a gastric ulcer, an ileus and possibly a diffuse vasculitis. In particular we might mention collagen diseases giving rise to hypersplenism and particularly lupus erythematosus. The spleen was not palpable, however, in this lady, though the abdominal distension could have masked an enlarged spleen. We would like very much to consider a single disease process being responsible for all of the physical and laboratory findings. Henoch-Schoenlein purpura would be a possibility since the platelets may be low in some of these individuals, particularly with an associated allergic type vasculitis. Thrombotic thrombocytopenic purpura could explain many of the findings; however, the patient showed no hemolytic anemia or central nervous system findings. She was also afebrile, and

this makes thrombotic thrombocytopenic purpura an unlikely explanation for this woman's problems.

Leuko-Erythroblastic Anemia

The peripheral blood smear which Dr. Trucker kindly provided revealed a leukopenia and a leuko-erythroblastic reaction. There were many immature granulocytes and myelocytes present in the peripheral blood, together with a number of circulating normoblasts. In addition to low platelets and anemia, we now have the problem of the differential diagnosis of a leuko-erythroblastic reaction. This reaction is seen with aplastic anemia, atypical leukemia, osteosclerosis and infiltrative processes of the bone marrow, such as metastatic carcinoma.

Gastric Carcinoma

With the history of gastric ulcer and the findings on the films of the pelvis, we would have to think of gastric malignancy. There was no radiologic evidence to support the diagnosis of gastric cancer. Nonetheless we must think of an occult gastric cancer in a patient with symptoms of increasing intensity, not relieved by routine ulcer management. Approximately 10% of gastric malignancies are found in patients below the age of 40 years, and so age does not help differentiate a benign from a malignant gastric ulcer. Other possible primary sites in this woman would include a carcinoma of the breast or ovary. A renal cell carcinoma could not be excluded, particularly in the presence of hematuria. The presence of leuko-erythroblastic anemia and a gastric ulcer makes me favor the diagnosis of gastric carcinoma with bone marrow involvement. "I think a bone marrow was the operation performed at the end of the protocol."

Dr. Robert McAllister's Diagnosis

1. Gastric carcinoma with bone marrow metastases.
2. Leuko-erythroblastic anemia due to bone marrow infiltration.

Pathological Discussion

Dr. Earl B. Trucker*:

The peripheral blood findings on admission, and particularly the profound thrombocytopenia, led to considerable discussion in our department. The spacing of the red blood cells on the peripheral smears suggested a moderate anemia; however, these cells appeared normochromic and normocytic. Considerable polychromasia was present and the red cells showed minimal poikilocytosis. Numerous Howell-Jolly bodies were encountered on the peripheral smear, together with occasional target cells. On counting 100 white blood cells, three to four circulating nucleated red blood cells were encountered. An example of the circulating normoblasts is seen in Figure 2. In addition, other occasional circulating cells were seen with a loose chromatin pattern and a small amount of deep blue cytoplasm. These cells could represent circulating tumor cells or so-called "Turk-irritation" cells. An example of such a cell is seen in

*Associate Pathologist, Hennepin County General Hospital. Dr. Trucker died of Hodgkins disease on November 26, 1966.

Continued

Figure 3. The blood platelets were markedly decreased and on many oil immersion fields no blood platelets were encountered. A leukopenia was present together with a shift to the left in the neutrophilic series. Many neutrophilic band forms showed toxic granulations and Dohle bodies.

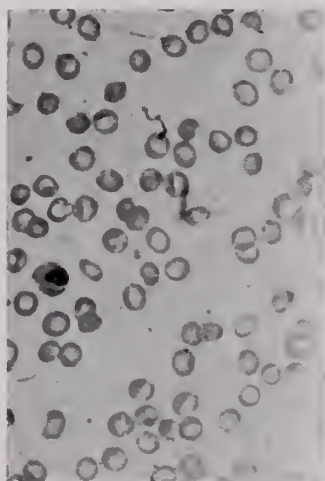


Fig. 2 — Circulating orthochromatic normoblast with pyknotic nucleus $\times 100$.



Fig. 3 — Turk-irritation cell with abundant blue cytoplasm and loose chromatin network in nucleus $\times 100$.

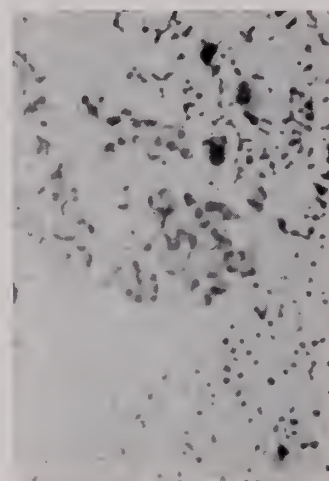


Fig. 4 — Metastatic signet-ring carcinoma to bone marrow sections — mucicarmine stain $\times 100$.

Dr. McAllister is quite correct in his assumption that the operation performed was a bone marrow examination. The direct smears of the bone marrow appeared slightly hypocellular with a myeloid erythroid layer of 7% and a red cell volume of 25%. The direct smears of the bone marrow showed more tumor cell clumps than I have ever seen. In most bone marrows I have reviewed, only a few carcinoma cells are seen and you are quite fortunate to identify them. The tumor cells here are not forming glands, but they are definitely of the signet-ring variety. Metastatic carcinoma to the bone marrow is the obvious explanation for the leuko-erythroblastic anemia. An example of the signet-ring cells, as seen on bone marrow aspiration, is presented in Figure 4, stained with a mucicarmine stain. Leuko-erythroblastic anemia was first well described by Vaughn¹ and the most common cause of that condition is an infiltration of the bone marrow by metastatic carcinoma. The association of thrombocytopenia with this syndrome has been documented in two similar cases recorded in recent years in the *New England Journal of Medicine*.^{2,3} In both instances a diagnosis of carcinomatosis was not made during life and both gastric lesions were initially missed on autopsy examination. Sections of areas of superficial gastric erosion verified the presence of signet-ring cells, infiltrating the submucosa of the stomach. Although in all likelihood the stomach was the primary source of the metastatic carcinoma in the bone marrow, we cannot give absolute confirmation since no autopsy was performed in this case.

Pathological Diagnosis

1. Metastatic adenocarcinoma to the bone marrow, stomach probably primary source.

2. Leuko-erythroblastic anemia, due to bone marrow infiltration by tumor.

*Associate pathologist. Director of the Bacteriology Department.

Robert L. Strom, M.D.*
Hennepin County General Hospital
Minneapolis, Minnesota

References

1. Vaughn, J. M.: Leuko-Erythroblastic Anemia. J Path Bact 42:541, 1936.
2. Case Records of the Massachusetts General Hospital (Case 57-1962). New Engl J Med 267:452, 1962.
3. Case Records of the Massachusetts General Hospital (Case 21-1963). New Engl J Med 268:672, 1963.

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Dr. Edwin Englert, Internist, Utah
- March 13 *The Use and Limitations of Therapy in the Management of Thrombosis*
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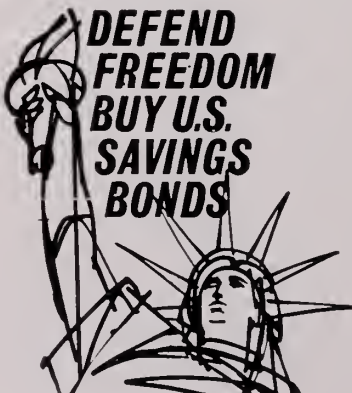
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Hart, Journal of Bone and Joint
Surgery, Vol. 31-A, pp 357-372,
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Grand Rounds

*Pulmonary Sarcoidosis**

DOUGLAS KJELLEN, M.D.
Medical Resident

Historical

The first description of sarcoidosis was made in 1875 by Jonathan Hutchison, who observed the granulomatous lesions on the skin of a patient and called the disease "Mortimer's Malady." In 1889 Besnier described a similar case which he called "lupus pernio," thinking the skin lesions were a form of tuberculosis (*lupus vulgaris*). In 1899 Caesar Boeck, a Norwegian physician, reported the first anatomic and clinical description of systemic sarcoidosis. In 1914 Schaumann showed that the diseases previously described by Besnier and Boeck were identical and that sarcoidosis was primarily a disease of the lymphoid system.

Since the first description of sarcoidosis, our concept of the disease has broadened from that of a disorder of the skin to a widely disseminated disease capable of involving all organ systems of the body and producing many hematologic, serologic and biochemical abnormalities.

Pathogenesis and Epidemiology

The pathogenesis of sarcoidosis is difficult to relate in the absence of a known etiologic agent. The disease is essentially worldwide in distribution, the highest incidence being reported in Sweden where up to 140 cases per 100,000 population occur in certain rural forested areas.¹ The heaviest concentration in the United States is in the southeastern states. There is an undisputed predilection for Negroes, among whom the disease has been reported to occur from 15 to 18 times as frequently as among whites. The peak prevalence of sarcoidosis is in the third decade of life. Although its occurrence is infrequent in the extremes of life, the diagnosis should be considered in older patients. Mayock et al.² emphasized that in 12% of a large series the age of onset was 50 years or later. While white males and

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, Minneapolis, July 12, 1966.

Continued

females appear to be affected about equally, negro females are affected with approximately twice the frequency of negro males.

Eskimos and Indians in Canada have little susceptibility to sarcoidosis in contrast to their high incidence of tuberculosis.³ The disease is rarely reported in the Chinese.

Etiology

Tubercle Bacillus

The specific cause of sarcoidosis has never been established. There is much dispute over the possible relationship to tuberculosis, and advocates of this etiology feel it is an aberrant form of tuberculosis: that the high incidence of negative tuberculosis reactions and the inability to isolate acid-fast bacilli from the lesions are due to an immunologic phenomenon such as a positive anergy.* More recently the suspicion cast upon the human tubercle bacillus is being shifted to the unclassified mycobacterium.³

Mankiewicz⁵ has postulated that certain lysogenic mutants of tubercle bacilli may be the causative agents; he has demonstrated that increased numbers of mycobacteriophages can be isolated from the stool, lymph nodes, and lungs of patients with sarcoidosis. When these phages act upon tubercle bacilli, lysogenic mutant forms can be produced. Sarcoid-like lesions can be produced in the guinea pig simultaneously infected with tubercle bacilli and mycobacteriophages.

Pine Pollens

Still more recently, the inhalation of various soil types and pine pollen have been suggested. Cummings et al.⁴ noted the close correlation between the birthplace of patients and the distribution of pine-forested areas. Their laboratory studies revealed pine pollen to have acid-fast characteristics similar to the tubercle bacillus, and when pine pollen was injected intradermally or subcutaneously in guinea pigs, a localized epithelioid cell granuloma was produced. This suggested a possible hypersensitivity to inhaled pine pollen as an etiology in some cases. Attempts to produce granulomas with pine pollen in patients with sarcoidosis have usually been unsuccessful.

Other investigators have related sarcoidosis to a variety of causes including viruses, mycotic infections, allergic or collagen-like diseases, syphilis and leprosy.

There are a number of organisms and physical agents which produce "sarcoid-like" granulomatous diseases. Among these are included a variety of fungi, lepra bacillus, zirconium, beryllium, pine pollen, specific soil types and certain hairsprays.

Pathology

Sarcoidosis is a protean disease characterized by the formation of non-caseating granulomas that may involve almost any organ or tissue of the body. The lymph nodes are most commonly involved, especially the hilar or tracheobronchial nodes, followed in frequency by the lungs, liver, spleen, skin, eyes and bones.

Histopathology

Microscopically the noncaseating granuloma is composed of large,

*See Test Your Word Score Page 221.

plump, closely packed, epithelioid cells surrounded by a scant rim of fibroblasts and a few scattered lymphocytes, with multinucleated giant cells interspersed throughout.⁶ Inclusion bodies have been described in the giant cells and are usually of two types: (1) asteroid bodies which are of yellow-brown granular structure with sharp ray-like filaments and may represent protein or metal deposits; (2) Schaumann bodies that resemble the corpora amylacea of the prostate.

Neither of these inclusions is pathognomonic, since similar ones are also found in beryllium lesions, nonspecific foreign body granulomas, early tuberculosis and certain fungal diseases. Caseation necrosis does not occur.

Coalescent Granulomas

The lesions may appear to be progressive, static or retrogressive. Coalescence of granulomas produces nodules of varying size visible macroscopically. In the lung, the lesions are distributed throughout the parenchyma, usually bilateral with some tendency to localize about blood vessels, bronchi and lymphatics. There is a tendency for the lesions to heal, leaving varying stages of fibrosis and hyalinization.

Although histopathology is extremely valuable in assisting in diagnosis, it is impossible to be unequivocal because of the inability to differentiate from Hodgkin's disease, lymphosarcoma, histoplasmosis and noncaseating tuberculosis, and other diseases in which noncaseating granulomas may be present. Thus pathologists can merely report the microscopic appearance to be compatible with sarcoidosis.

Clinical Features

The outstanding clinical feature of sarcoidosis is the disparity between the mildness of symptoms and the extensive involvement of the various organs. Sarcoidosis usually commences in an insidious manner; often attention is first drawn to the presence of the disease following a routine x-ray of the chest. As the disease progresses, symptoms invariably appear and usually consist of weight loss, fatigue and vague respiratory complaints including cough, breathlessness and chest discomfort.

Pulmonary

The frequency of systemic and respiratory symptoms in 160 patients with sarcoidosis are recorded in Table 1.⁷ As pulmonary function is

TABLE 1*
Frequency of Systemic and Respiratory Symptoms
In 160 Patients with Sarcoidosis

	Percent With Symptom
Weight loss	54
Fatigue	44
Joint and muscle pain	9
Fever	6
Cough	51
Breathlessness	39
Chest pain	29
Hemoptysis	7
No symptoms	11

*From Israel, H., M. Sones: Arch Intern Med 102:766, 1958.

Continued

compromised, dyspnea may reach major proportions with extensive involvement, productive cough and hemoptysis.

Hemoptysis in sarcoidosis is infrequent and massive pulmonary hemorrhage is rare. Its occurrence is attributed to concurrent pulmonary disease or a complication of sarcoidosis such as bronchiectasis. Massive fatal hemorrhage has been reported in six cases and is probably due to granulomatous invasion of the pulmonary vessels.⁸

Fever

Fever, if present, is usually low grade and occurs during periods of greatest activity of the disease. The mere presence of respiratory symptoms in pulmonary sarcoidosis signifies rather extensive involvement of the lungs.

There is usually a paucity of physical findings as compared to radiographic findings. Occasionally fine respiratory rales or scattered wheezes may be heard.

Pulmonary Involvement

The lungs are involved in approximately 90% of patients with sarcoidosis as evidenced on chest x-ray, and this would probably approach 100% if routine blind lung biopsies could be done on all cases. Even in the absence of symptoms or parenchymal abnormality on chest x-ray, almost all cases show impairment of pulmonary function indicating lung involvement.⁹ The type and degree of pulmonary involvement determines whether the patient will recover or be left with significant respiratory impairment.

Intrathoracic Stages

Siltzbach¹⁰ has classified the intrathoracic lesions by stages. *Early or Florid Stage*: a. Bilateral symmetric hilar node enlargement, usually asymptomatic and detected by routine chest x-ray. Disseminated pulmonary disease although not visible on x-ray may be shown by lung biopsy and decreased pulmonary function. b. Widely disseminated or localized fine miliary and occasionally gross miliary nodulation with hilar node regression or persistence. Patients with miliary lesions on the presenting chest film tend to have a poorer prognosis than those with only hilar node involvement. c. Diffuse bronchopneumonia infiltrations. *Transitional Stage*: Infiltration of the pulmonary interstitial tissue with granulomas and fibrous tissue causing a fine or coarse reticular appearance. Mild degrees of emphysema may be present. *Late or Fibrotic Stage*: Dense fibrosis and hyalinization of the granulomatous lesions occur. There is retraction of the lung roots with fibrous strands and nodules of varying sizes. Giant bullae and advanced emphysema may be superimposed.

Enlarged Hilar Nodes

Enlargement of the hilar nodes, usually bilateral, occurs in most cases of pulmonary sarcoidosis and varies from a slight increase to huge so-called "potato nodes." Although hilar adenopathy alone usually causes no symptoms of bronchial obstruction, mainly because of absence of inflammatory reaction around the nodes, an occasional case of airway obstruction has been reported. The bilateral hilar adenopathy syndrome occurs mainly in young adults, predominantly females, many of whom present with erythema nodosum accompanied by pain and swelling of the joints,

especially the ankles. In those without erythema nodosum, the joint pains are unusual.

Infiltration of the parenchyma of the lung produces a wide variety of both clinical and radiological pictures. Lesions are usually small and discrete but coalesce to form larger nodules widely scattered throughout the lungs, mimicking miliary tuberculosis but occasionally restricted to more localized areas. Extensive involvement may occasionally be seen in patients who are completely asymptomatic; and it is again stressed that there is little correlation between clinical findings and the roentgenologic appearance. The activity of sarcoidosis likewise cannot be determined on the basis of the x-ray appearance.

An unusual type of pulmonary disease is represented by large discrete nodules resembling metastatic carcinoma of the "cannon ball type" in combination with varying degrees of more typical pulmonary involvement.¹¹ Cullen and co-workers¹² report four cases presenting with diffuse pulmonary infiltrations manifesting primarily as airway obstruction. Pleural involvement is an uncommon finding in sarcoidosis.¹³

Abnormalities of Pulmonary Function

Previous studies have shown that the major abnormality in pulmonary function is reduction of the diffusion capacity. Less frequent defects have been reduced lung volume, reduced compliance, decrease in maximal breathing capacity and increased airway resistance.

Diffusion abnormalities are explained on the basis of perivascular and alveolar fibrosis, compliance defects by interstitial fibrosis, and air flow obstruction by peribronchial fibrosis.¹⁴ Alveolar capillary block may be evident in many advanced cases of sarcoidosis.¹⁵

Abnormalities of pulmonary function seem to bear no definite relationship to the degree of parenchymal involvement reflected by chest x-ray. As might be expected, extensive perivascular fibrosis and anoxia lead to the development of pulmonary hypertension and cor pulmonale.

Ting et al.¹⁶ studied the mechanics of breathing in 31 patients with extensive parenchymal lesions. They found that when the x-ray showed evidence of extensive fibrosis, then diffusion capacity, lung compliance and lung volume were impaired. When cystic or bullous changes were present, airway obstruction could be demonstrated by increased pulmonary resistance and a decrease in maximal mid-expiratory flow rate. Whereas restrictive changes and impaired gas exchange are the most frequently demonstrated pulmonary function abnormalities, small airways are frequently narrowed by peribronchial fibrosis. Reduction in compliance is associated with diminished vital capacity and is probably the major cause of dyspnea.¹⁶

Laboratory Data

Laboratory findings are neither pathognomonic nor consistent enough to afford great diagnostic value. Aberrations of serum proteins occur in about 50 to 70% with a "step-like" electrophoretic pattern, increases in α_2 , B, and γ globulin and an occasional decrease in albumin being frequently reported. Series including a predominance of Negroes show a higher frequency of hyperglobulinemia. It is interesting to note

Continued

that in a large series of 246 patients reported from a white European population, the electrophoretic pattern was abnormal in only 34%, with increase in γ and α_2 globulin being the most frequent, with only one patient showing a step-like rise in the globulin pattern.¹⁷

Eosinophilia of greater than 5% occurs in 20% to 30% of cases. The eosinophilia sedimentation rate is elevated in those with active disease, especially during febrile periods. Serum Ca. has been found to be elevated in 20% to 30% of cases and is not associated with osseous involvement. Elevated serum alkaline phosphatase and cephalin flocculation are frequently noted. Leukopenia is present in approximately 30% of cases, and occasionally thrombocytopenia is seen.

Skin Tests

Insensitivity to tuberculin testing is a major feature of sarcoidosis. Patients may react to tuberculin before the onset of sarcoidosis, fail to react during the course of the disease and regain tuberculin sensitivity on recovery. Some feel the depressed skin reactivity is due to an impaired immunologic mechanism caused by the systemic lesions. Others support the hypothesis that the inability to develop delayed hypersensitivity is a constitutional defect that is prerequisite to the development of sarcoidosis.¹⁸ British investigators have claimed that tuberculin sensitivity is not absent but merely suppressed in most cases and may be unmasked by the addition of cortisone to the tuberculin skin-testing material or the use of depot tuberculin.¹⁹

Bacillus Calmette-Guerin Vaccination

An extensive study by Sutherland et al.²⁰ in Great Britain, in which more than 54,000 young adults participated in a trial of tuberculosis vaccines, revealed that tuberculosis vaccination at age 14 neither protected against sarcoidosis *nor promoted this disease*, and the incidence of sarcoidosis in this population group was not influenced by the initial tuberculin status of the participant. Children in this series who failed to develop tuberculin sensitivity after two Bacillus Calmette-Guerin vaccinations, and were seemingly healthy were given Kveim tests, with a high proportion showing positive reactions.

Israel and Sones²¹ found that Bacillus Calmette-Guerin vaccination did not affect the Kveim reaction and that in patients recovered from sarcoidosis the vaccine could not induce tuberculin sensitivity.

Kveim in 1941 demonstrated that the intracutaneous injection of a saline suspension of sarcoid lymph node into a patient with sarcoidosis resulted in the development of a papule within one to four weeks. On biopsy its histology was that of the "sarcoid reaction." The Kveim reaction is positive in the vast majority of cases. The conflicting reports concerning its significance stem from the unpredictability of the antigen and from difficulty in its standardization.²² The Kveim test yields a variable number of false positives and may fail to detect from 20 to 25% of individuals with sarcoidosis. The incidence of positive reactions is greatest in early cases, decreasing with chronicity of the disease and becoming negative in a high percentage of inactive cases.

The recent report of successful transfer of Kveim reactivity to normal individuals by giving leukocytes from patients having sarcoidosis suggests

it may be an antigen-antibody reaction.²⁴ Limitations of the Kveim test are:

1. Scarcity of the antigen.
2. Difficulty in standardizing the material.
3. Occasional deterioration, which may eventually impair potency and specificity.

Biopsy

Diagnosis depends on anatomic pathological biopsy confirmation, a consistent clinical picture, and the exclusion of other diseases giving a similar picture.²³

Enlarged peripheral lymph nodes, cutaneous lesions, enlarged liver and spleen, lung and scalene fat pad are all excellent biopsy sources. Less commonly used sites are the gastrocnemius muscle, lacrimal glands, conjunctivae, tonsils and bronchial epithelium.

Mediastinoscopy has proved valuable in the diagnosis even when chest x-ray has not shown any widening of that region, and biopsy results from several series are most impressive (Table 2).²⁴ The bone marrow has not been of great diagnostic value, showing granulomas in less than 30% of cases.

TABLE 2*
Sarcoidosis

Author	Bronchoscopy		Prescalene Node		Mediastinoscopy	
	# of Pts.	Posi- tive	# of Pts.	Posi- tive	# of Pts.	Posi- tive
1. Friedel et al.	86	10.5%			30	100%
2. Lofsgren et al.			47	32%	34	94%
3. Maasen	52	35%	26	62%	59	100%
4. Bergh et al.					33	100%
5. Carlens	56	20%			123	96%

*From Carlens, E.: *Ann Otol* 74:1102, 1965.

Course and Prognosis

The clinical course is quite unpredictable in the individual patient. In 25 to 50% of the patients, the disease runs its course over several years with eventual recovery. In another 20 to 35% some improvement occurs, but these patients are left with some functional impairment. Five to 15% tend to become worse with development of rather severe respiratory impairment. Five-year survival rates are quoted as 85 to 90% with most deaths due to pulmonary fibrosis, respiratory failure, pulmonary hypertension and cor pulmonale. Skin lesions of erythema nodosum, especially when associated with hilar adenopathy, tend to carry a good prognosis. Extrapulmonary manifestation, cutaneous and osseous lesions are associated with a poor prognosis.

Treatment

Recent attention has been focused almost entirely upon the use of corticotropin and corticosteroids. The active or proliferative stage of sarcoidosis shows the most dramatic response to these drugs. Systemic steroids are suppressive rather than curative, and initiation of treatment shortly after onset of the disease does not seem to prevent residua or

Continued

change in x-ray appearance. Lewis et al.¹⁵ reported that patients treated early with steroids had the mildest symptoms and functionally had diffusion abnormalities but not compliance or ventilatory defects. Steroids seem to suppress the granulomatous inflammation as well as the associated symptoms. Withdrawal of these drugs is followed by a recurrence of symptoms and worsening of the lung lesions, especially in the chronic case. Duration of therapy is variable and often a matter of trial and error, but in general, course of therapy should exceed two to three months. There are conflicting views on whether or not patients receiving steroids for sarcoidosis should be covered with antituberculous drugs.

Antimalarial drugs have also been used with reports of varying success.

Case Report

A 27-year-old negro female was admitted to Hennepin County General Hospital on May 10, 1966, complaining of shortness of breath of two weeks' duration. For ten days prior to admission she had noted intermittent pleuritic-type pain in the anterior mid-chest accompanied by a nonproductive cough and episodes of chilliness. She had been bothered by perennial attacks of wheezing and dyspnea since infancy. These attacks were usually precipitated by upper respiratory infections and were more frequent during the winter months. The patient had been diagnosed as having intrinsic bronchial asthma, and it is noted that all previous attacks had responded readily to the usual treatment, leaving the patient completely asymptomatic.

The patient had moved to Minnesota from Monmouth, Illinois, about ten years ago. She smokes one pack of cigarettes per day.

Physical examination revealed a well-developed, young negro female, in no apparent distress. Her oral temperature was 100 degrees F., blood pressure 90/60 mm. Hg., and pulse 108 per minute. Examination of the ears, nose and throat was negative, as was the fundusoscopic examination. Lacrimal and parotid glands were normal. There were bilateral enlarged anterior cervical nodes. Diminished breath sounds and fine rales were heard at the right base; later a pleural friction rub was audible over the right mid-lung field. Examination of the heart and abdomen was negative. No skin lesions were present.

Laboratory values: hemoglobin 12.6 gm. %, white blood count 8,000 with normal differential. Eosinophils were not increased. Erythrocyte sedimentation rate was 70 mm/hr. The urinalysis was negative. The serum calcium was 9.5 mgm. %, serum proteins 6.5 gm. % with albumin 3.8 gm. % and globulin 2.7 gm. %. Serum protein electrophoresis showed a borderline elevation in α and γ globulin and a decrease in the albumin fraction. BSP. retention was 8%, cephalin cholesterol flocculation negative and alkaline phosphatase normal. Mantoux skin tests were negative. Both skin tests and complement fixation tests with histoplasmin, coccidioidin and blastomycin were negative. Chest x-ray showed hilar node enlargement and bilateral pulmonary infiltrates involving the mid-lung fields. X-rays of the hands and feet were negative. An EKG. was within normal limits. Biopsy of the liver revealed multiple noncaseating granulomata. The Kveim intradermal skin test antigen was injected intradermally on 6/2/66; the resultant papule biopsies on 6/29/66 were read as positive. A right scalene node biopsy revealed numerous noncaseating granulomas compatible with sarcoidosis.

Pulmonary function studies revealed reduced maximal breathing capacity and total vital capacity with normal timed vital capacity consistent with mildly decreased compliance. Gas diffusing capacity was not determined.

References

1. Atwood, W. G., C. T. Nelson: Med Clin N Amer 49:783, 1965.
 2. Mayock, R. L., P. Bertrand, C. Morrison, and J. Scott: Amer J Med 35:67, 1963.
 3. Siltzbach, L. E.: Amer J Med 39:361, 1965.
 4. Cummings, M., and M. Michael, Jr.: DM, May, 1960.
 5. Mankiewicz, E.: Canad Med Ass J 88:593, 1963.
 6. Robbins, S. L.: Textbook of Pathology 384, 1957.
 7. Israel, H., and M. Sones: Arch Intern Med 102:766, 1958.
- 8-24 May be secured from the Grand Rounds Editor.

Derivatively Speaking

Syndrome — from Greek *syn* (with) plus *dramein* (to run)



Abstracts, Briefs and Commentaries

SURGICAL DISEASES OF THE CELIAC AND MESENTERIC ARTERIES

The author discusses the symptoms, signs and surgical treatment of occlusive processes of the celiac and mesenteric arteries. Etiology of the occlusive process includes atherosclerosis, emboli, trauma and congenital lesions as well as others.

In general, symptoms are characteristic — cramping postprandial abdominal pain, intermittent or constant, and made worse by large meals. There may be constipation early, later diarrhea. Weight loss is common. An abdominal bruit is often heard. A *lateral* aortogram is diagnostic.

The various surgical techniques to relieve the occlusive disease is well described. Special attention in the postoperative management is directed to (a) use of antibiotics, (b) the chronic malabsorption syndrome which slowly relents, and (3) the development of intestinal stricture secondary to the ischemia.

Comment: Abdominal angina is a treatable disease. A high index of physician suspicion is the key to the diagnosis.

Jerome T. Grismer, M.D.
Minneapolis, Minnesota

Rob, Charles: Surgical Diseases of the Celiac and Mesenteric Arteries. Arch Surg 93:21, 1966.

A NEW METHOD FOR DETECTION OF THE LEAKY GLOVE

In a rather intriguing manner the authors discuss their technique of discovering holes in surgical gloves — an electrical glove testing unit. The insulating effect of the surgical glove is negated as sterile saline contacts the skin of the surgeon, completing a circuit. A flashing light signifies the contact.

Two hundred and ten presterilized disposable gloves were tested preoperatively: 1.4% (3) were defective. Two hundred and thirty checks were performed during or after the procedure; 35% (80) gloves were defective.

The fingertips of the surgeons were plated on agar after the surgical scrub with commercial solutions and at the close of the procedure. Of

Continued

these 306 at each time, 161 plates had more, 63 had the same, and 82 had less bacterial growth postoperatively. Usually the bacteria was *S. epidermides*, and this was often found in postoperative wound infections.

Comment: Although not new, an ingenious detection unit that can be incorporated in every hospital.

Jerome T. Grismer, M.D.
Minneapolis, Minnesota

Russell, T. R., Roque, F. E., Miller, F. A.: A New Method for Detection of the Leaky Glove. *Arch Surg* 93:245, 1966.

SUCCESSFUL USE OF DEXTRAN IN PHLEGMASIA CERULEA DOLENS

The varied treatment of massive venous thrombosis, the serious nature of the disease and the post-treatment morbidity are briefly reviewed. The rationale for use of Dextran 75 is related to several factors: (a) adherence to the vessel intima as a negatively charged mononuclear layer, which increases the zeta potential and negative electrical charge on the formed blood elements, increasing repellency and decreasing sludging, (b) inclusion of Dextran into the red blood cell envelope, altering the abnormal reaction of disease and reducing the bonding action, (c) inhibition of clotting by insulation of the coagulation reactants from each other, and (d) other results of osmotic properties on blood volume, cardiac output, etc.

The author describes the type and indications for therapy with Dextran 40 and 75 in five patients. Prompt improvement in signs and symptoms was noted in each.

Comment: The discussion of this article is as important as the article. My own experience has been favorable. This, however, is not a general opinion.

Jerome T. Grismer, M.D.
Minneapolis, Minnesota

Levy, J. S., Tryspel, O. H., Bergen, J. J.: Successful Use of Dextran in Phlegmasia Cerulea Dolens. *Arch Surg* 93:33, 1966.

A NEW METHOD FOR DETECTION OF THE LEAKY GLOVE

Bacteria on the surgeon's hands cannot be totally obliterated by a scrubbing technique. The only barrier between the surgeon's hands and the wound is the intact surgical glove. The finger tips of surgical teams have been plated after a ten-minute scrub with antiseptic soaps. Plating was repeated after surgical operation following the removal of the gloves by a nurse. The plates were incubated for 48 hours and rated from grade 0 to 4. Grade 4 showed a growth of more than 30 colonies. Two hundred and ten standard, pre-sterilized, disposable gloves were tested immediately after the surgeon was gloved, and 1.4% were defective. A total of 80 defective gloves was found among 230 checks during or immediately after surgery (35%). Of 44 cases studied, 79 percent of either the surgeon or his assistants developed a defective glove before the operation terminated. In nine cases which lasted under one hour, five had a member of the team with a defective glove when the procedure terminated (55%). In 35 procedures lasting more than 60 minutes, 85 percent had a defective glove.

Cultures revealed the staphylococcus epidermidis as the most frequent bacterial growth but occasionally the hemolytic *S. aureus* was isolated. The authors, in a review of the literature, found the percentage of perforated gloves to vary from 10% to 30%.

The equipment used by the authors to detect perforated gloves while on the hands of the surgeon and assistants seems quite simple. The fact that the glove is nonconductive is the basis of the test. A sterile basin partially filled with salt solution is placed on the electronic stand, which is grounded to the conductive floor. The circuit is open. When the surgeon with conductive shoes places a hand with a defective glove in the basin the circuit is completed and a light flashes. A hole in the glove can be localized, even to which finger is defective.

One group in the United States and a second group in England had described equipment based on the same electrical principle.

The authors also state that because of their concern on the adequacy of scrubs, they had medical students scrub for 30 minutes with various antiseptic agents. They concluded that it was virtually impossible to remove all bacteria from the skin.

With their equipment close to the field of surgery, members of the team can test their gloves at intervals during operations.

COMMENT: I have no doubt that every surgeon has been concerned about holes in his gloves and those of his team. He is well aware of the fact that he cannot sterilize his hands either mechanically or chemically. By this method which seems quite simple and efficient, one source of infection, though not eliminated, could be detected early. Their surgical team tests their gloves for leaks frequently during surgery.

Stanley R. Maxeiner, Sr., M.D.
Minneapolis, Minnesota

Russell, Thomas R., Roque, Francis E., and Miller, Fletcher A.: Omaha, Nebraska. Arch Surg, August, 1966.

CARDIAC CATHETERIZATION

These individuals have succinctly described their objections to a recent editorial "Use and Abuse of Cardiac Catheterization" — J. L. Ankeney, Annals of Thoracic Surgery 5, 660, 1965. In their letter, these authors point out the need for accurate assessment of the cardiac problem not possible by conventional means. They also indicate that postoperative evaluation of surgical results is objectively served by cardiac catheterization. To summarize their letter — "The more completely the patient is studied, the better prepared is the surgeon to do his best with the most possible benefit occurring to the patient —".

COMMENT: The original editorial of J. L. Ankeney and the above correspondence deserve more attention. Cardiac catheterization can be performed with much greater safety than a cardiac operation or exploration. It is difficult for me to adopt the philosophy that complete study is not needed. One can only agree with Drs. Zimmerman and Demany.

J. T. Grismer, M.D.
Minneapolis, Minnesota

Zimmerman, H. A., and Demany, M.: Correspondence. Ann Thorac Surg 2:876, 1966.

PSYCHOSOMATIC PREDISPOSING FACTORS IN ALLERGIC DISORDERS

In this investigation, the authors examined 65 male college students, 41 of whom had been independently diagnosed as having allergies, and 24 of whom had been independently diagnosed as being free of allergies. Each student was examined for the presence of a somatic allergic predisposition by giving skin tests and a Histamine Challenge Test. Likewise, each student was examined for the presence of a psychological allergic predisposition by using a Parent-Child Questionnaire and a Family Interaction Test.

According to the authors' criteria, the allergic students had a greater somatic and a greater psychologic predisposition than the nonallergic students. Somatic factors indicating an allergic predisposition were found in 92% of the allergic and 33% of the non-allergic students. Psychologic factors indicating a psychological predisposition were found in 78% of the allergic and 50% of the non-allergic students. Both a psychological and a somatic predisposition were found in 75% of the allergic and in 25% of the non-allergic students.

On the basis of their findings the authors conclude that both somatic and psychologic factors are present in allergic illnesses. They speculate that the psychological factor of critical importance is a childhood experience of exaggerated dependency highlighted by maternal domination of the family. However, they also suggest that perhaps no specific psychological factor differentiates an allergic from a non-allergic patient.

COMMENT: This investigation confirms the sensitivity of allergic patients to histamine and to antigens. The evidence for a psychologic predisposition was not as strong. While a pathological degree of dependency may complicate or precipitate an allergic disorder, it is by no means proven that psychological factors cause these illnesses.

James Janecek, M.D.
St. Paul, Minnesota

Jacobs, M. A., Friedman, S., Franklin, M.D., Anderson, L. S., Muller, J. J., and Eisman, H. D.: Incidence of Psychosomatic Predisposing Factors In Allergic Disorders. *Psychosom Med* 28:679, 1966.

Buckle Up

High Speed and Bad Weather Don't Mix

Slow down for rain and fog.

Modern roadways don't eliminate danger in poor weather conditions.
Slow down.

High speed + bad weather + longer stopping distance = trouble.

You may drive into a fog pocket quite unexpectedly, and rain reduces visibility and causes your car to actually *float* on the highway.

It's as old as Adam: the law of self-preservation. It's as old as Eve: the law of self-interest. Combine 'em and you win! — Sales Management

The biggest block to many a man's success is his head. — Everybody's Weekly

The Doctor's Workshop

Cardiopulmonary Resuscitation in the Community Hospital

ROBERT S. ELIOT, M.D., F.A.C.P.*

DAVID ROSEN, M.D.**

JEROME GRISMER, M.D.†

Minneapolis, Minnesota

THE VALUE OF an organized program in cardiopulmonary resuscitation is well established in large hospitals.^{1,2} Little attention, however, has been paid to the development of a workable program tailored to meet the specific needs of a community hospital. The employment of resuscitation measures by several lay and paramedical groups has already demonstrated a beneficial effect.^{3,4} Increasing public and medical interest now indicates the need for a plan of attack when cardiac arrest occurs in the community or in the community hospital.

It is recognized that a variety of illnesses are treated in a community hospital. The number of admissions for acute myocardial infarction may be small and inconsistent. A workable program then should be designed for not only acute myocardial infarction, but also for other illnesses requiring careful and continuous observation and treatment.

The purpose of this communication is to set forth an organized plan for cardiopulmonary resuscitation in the community hospital. The background for this has been developed from a study of the programs which now exist or are under development in certain community hospitals in Minnesota.

The problems of organization in a community hospital to handle cardiac arrest can conveniently be broken down into three areas: equipment, personnel, and a plan.

Equipment

Equipment has been over-emphasized. Too much attention has been paid to expensive electronic monitoring apparatus when, in fact, only simple and relatively inexpensive equipment is needed.

Of prime importance is equipment designed to secure and maintain an airway. Plastic oral airways and nasal catheters should be available. Laryngoscope and endotracheal tubes are required. Tracheotomy kits should be made up in advance. A hand resuscitator, such as the Ambu or PMR, is convenient. Adequate suction must be available. All of the above-mentioned can be found in any hospital.

The significant point is that an emergency cart must be organized in advance to include this and other equipment (Figure 1). It is obvious that cardiac emergencies arise not only in the intensive care units or the hospital wards, but may also happen anywhere within the confines of a modern hospital. An appropriate number of carts then can be strategically located throughout the hospital and moved to handle cardiac arrest whenever and wherever it occurs.

Electronic equipment should be kept to a minimum, but the defibrillator is necessary. Much controversy over AC versus DC defibrillation can be found in the literature, but there has been no documented superiority in the termination of ventricular fibrillation and, therefore, either type will do.^{2,5,6} The anterior-posterior paddles are preferred. A cardiac monitor is valuable in following a

Continued

This study was supported by a research grant from the Minnesota Heart Association.

*Assistant Professor Department of Medicine, University of Minnesota.

**Assistant in Medicine, University of Minnesota.

†Mount Sinai Hospital, Minneapolis, Minnesota.

patient from moment to moment. For the purposes of a community hospital this should be a simple piece of equipment. Complicated pulse monitoring devices, automatic memory loops, and read-out devices are not necessary. The monitor should be one with which all the physicians and pertinent hospital nurses can easily become familiar. It should also be purchased from a company that can give adequate maintenance and repair.

It would perhaps be appropriate to comment on the relationship between a program in cardiopulmonary resuscitation and coronary care units. The value of coronary care units in reducing the mortality from acute myocardial infarction can no longer be questioned.^{7,8} The reduction occurs primarily in earlier detection and more rapid treatment of cardiac arrhythmias. However, regardless of the electronic sophistication of the units,

they are only as good as the personnel that staff them, and in turn their ability to handle cardiac arrest. The community hospital must handle all types of medical problems and in most instances cannot devote the space or personnel to develop a pure coronary care unit. Yet if one has (1) a good emergency cart, (2) a monitor and defibrillator and (3) medical and nursing personnel instructed in the technique of closed chest massage, the essential ingredients of a coronary care unit are all available within the framework of a more general intensive care unit.

It is also recognized that there are disadvantages in putting coronary patients into active and noisy intensive care units. Unfortunately, the alternative is usually to have no coronary care facility. Thus the intensive care unit becomes the better choice. Most of these units have a "quieter" area where one

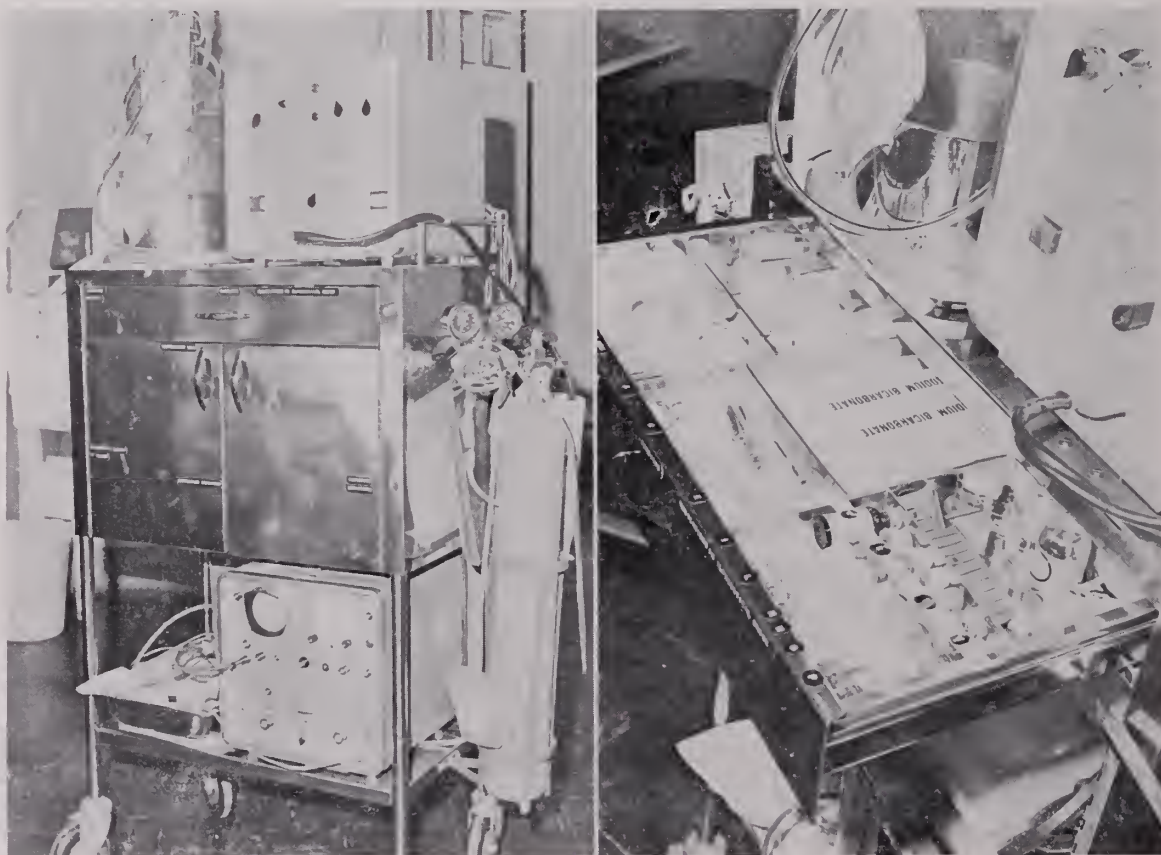


Fig. 1 — (Left) Cardiopulmonary resuscitation cart demonstrating defibrillator, monitor, oxygen, suction apparatus, and medicine cart. (Right) Same cart as above demonstrating emergency drugs in opened drawer on cart. (Both photographs kindly submitted by Dr. Marcus Keil, Albert Lea, Minnesota).

or two beds can be designated as coronary care beds and continually monitored. In this way the hospital can utilize existing facilities and personnel to provide a service which fits the needs of the community. This approach appears more reasonable than taking a pre-packaged coronary care unit and cramming it into the existing facility.

Personnel

In this outline to be presented, the authors have adapted a plan which has worked well in a 250 bed hospital. The authors are presenting this as a guide only. Each hospital must view this from its particular vantage point.

Five Groups

There are five groups, each with a specific responsibility, which converge on the patient's bedside when the emergency signal is flashed.

The monitor — The defibrillator console is under the responsibility of the Central Supply (C.S.). The unit is stored in C.S., and repairs, etc., ordered through C.S. At the signal, this unit is brought immediately to the floor, an elevator key (on the unit) speeding the delivery.

Special drug cart — This is also under C.S. responsibility. Drugs and supplies are under constant inventory, especially after a "run." Thus the two main units are in one area for storage.

The anesthetist or anesthesiologist comes immediately with the necessary endotracheal airways and small anesthesia machine for ventilation. A ventilating unit should have a manual as well as an automatic control so as not to oppose manual cardiac massage.

Laboratory technician with an electrocardiograph. This same technician is available to return to the laboratory with blood samples, etc. This machine can be monitored by the nurse or physician if necessary.

Nursing Supervisor and one other nurse to carry out drug infusion, assist in massage, etc. These two (or better three) are most important to the physician who, if alone, must do the massage, insert an I.V. cut down (intra cath-medicut), etc. Nurse's aides or

orderlies can be trained in massage to assist the physician.

The Patient

In order of importance, the patient has: (a) an airway established, (b) cardiac massage, and (c) an intravenous route inserted to allow drug infusion. Once these three points have been accomplished, the patient is "under control" and the success or failure of the resuscitation will depend on many other variables.

Medical Plan

The Clinical Findings and Treatment in Cardiopulmonary Arrest

The patient who experiences cardiopulmonary arrest may be the victim of one of three major forms. The first is *cardiac standstill*; the second is a *ventricular arrhythmia*; and the third is *systemic collapse* or *shock*. Auscultation is frequently unrewarding since the patient with cardiac arrest or ventricular fibrillation may give no auscultatory evidence of cardiac action. Both the pulse and heart beat are often present, however, in the patient with peripheral circulatory collapse.

The presence of dilated pupils indicates that cardiopulmonary arrest has existed for more than a period of one and one-half minutes. Constriction of the pupils may indicate that the patient is either on drugs (such as morphine) or that cardiac arrest has occurred within a matter of 45 seconds. The following steps are useful in approaching the patient with suspected cardiopulmonary arrest.

STEP 1. The timetable following the loss of heart beat.

A. The loss of major pulses.

B. The loss of respiration (occurs 30 to 45 seconds following cardiac arrest).

C. Dilated pupils occur 45 seconds to 1½ minutes following cardiac arrest.

STEP 2. The institution of ventilatory resuscitation.

A. Mouth-to-mouth.

B. Mouth-to-nose.

C. Mouth-to-airway. (Endotracheal intu-

Continued

bation if possible, but do not delay until necessary equipment is available.

STEP 3. The institution of circulatory resuscitation.

A. External cardiac massage.

STEP 4. Identify the type of cardiac arrest by use of the electrocardiogram.

A. Asystole is indicated by the presence of a straight line on the electrocardiogram.

B. Ventricular fibrillation is indicated by a series of wiggly lines without a QRS complex.

C. Profound cardiovascular collapse is indicated by the presence of normal QRS configuration by the finding of decreased blood pressure and so forth.

STEP 5.

Involves a series of alternate treatment depending upon the type of cardiac arrest occurring.

ALTERNATE STEP 5. Treatment of asystole.

(The treatment of asystole includes complete heart block and severe sinus bradycardia since they present similar pathophysiologic states).

A. Percuss the chest.

B. Direct intracardiac injection of epinephrine (3 to 5 cc. of 1 to 10,000 solution).

C. Substitute isuprel (0.02 to 0.4 mg. every five minutes).

D. Substitute calcium chloride (3 to 10 cc. of 10 per cent solution every three to five minutes).

E. Always employ sodium bicarbonate (1 ampule every 5 minutes).

ALTERNATE STEP 5. The treatment of ventricular fibrillation.

A. Immediate A.C. or D.C. shock. Keep in mind the proper placement of electrodes. The use of the anterior-posterior electrode may be of considerable value here. One should employ an adequate amount of paste without unduly spreading it throughout the chest. Observe safety precautions, since incidental shock of the operator and assistants has occurred in several instances.

B. The use of I.V. procaine amide in 200 mg. increments or quinidine in 200 mg. increments should be instituted for refractory fibrillation.

C. If above methods fail, one might try 50 to 100 mg. of xylocaine intravenously with additional equal increments every five minutes to a maximum of 300 mg.

D. If defibrillation fails, D.C. counter-shock as well as the above measures may be attempted again. The operator should keep in mind that the anoxic myocardium cannot be defibrillated. Adequate oxygenation is tantamount to resuscitation.

E. Continue to use an ampule of sodium bicarbonate every five minutes.

ALTERNATE STEP 5. The treatment of profound cardiovascular collapse.

A. Employ the use of cardiotonic drugs, such as isuprel in the same doses as indicated for cardiac arrest.

B. Try vasopressor agents such as aramine or, in profound refractory collapse, levo-phed.

C. Use of large amounts of steroids up to 100 mg. of prednesone or 1 gr. of hydrocortisone.

D. Continue the use of sodium bicarbonate (1 ampule every five minutes) to prevent acidosis.

STEP 6. Post resuscitation treatment.

1. Constant electrocardiographic monitoring by use of an oscilloscope monitoring system.

2. Vital signs.

3. Assisted ventilation by intermittent positive pressure or artificial respiration if indicated.

4. Measurement of intake and output.

5. Maintenance of blood pressure capable of sustaining adequate urine output and consciousness.

6. Hypothermia if available has occasionally been shown to be of some value in this situation.

STEP 7. Recognition of complications of external cardiac massage.

It has been reported by several observers that rib fracture, cardiac contusion, laceration of the liver, severed blood vessels, bone marrow emboli, sternal fracture, laceration of the spleen, and the development of the flail chest can occur in patients treated by techniques of cardiac massage.^{4,9} These complications can be kept at an absolute mini-

mum if appropriate techniques are employed.

If the above methods are implemented, a survival of approximately 25 per cent of all in-hospital cases of cardiac arrest can be achieved.^{8,10,11} It should be recognized, however, that some patients will have residual neurologic and cardiovascular injury. Roughly 75 per cent of patients achieving cardiac resuscitation will leave the hospital in a satisfactory physiologic state.^{7,11}

Summary

This report presents a workable program for cardiopulmonary resuscitation in the community hospital. Included is an organizational outline covering personnel, equipment, and a plan of action. It is hoped that this approach will serve the interests of the community hospital which is charged with

the responsibility for care of patients with other serious illnesses as well as coronary artery disease.

Appendix

The basic emergency cart equipment includes:

- A. An airway
- B. Tracheotomy kit
- C. Hand Resuscitator (Ambu or PMR)
- D. Emergency drugs (as outlined in text)
- E. Oscilloscope and A.C. or D.C. cardioverter
- F. Suction apparatus

The authors will answer by mail or telephone any inquiries regarding specific problems by interested physicians and professional personnel. They also wish to express appreciation to the Minnesota Department of Health in deferring some of the travel expenses.

References

1. Day, H. W.: A Cardiac Resuscitation Program. *J Lancet* 82:153, 1962.
2. Phyllips, J. H., Burch, G. E.: Management of Cardiac Arrest. *Amer Heart J* 67:2:265, 1964.
3. Braun, P., Rertman, N., Florian, A. A.: Closed Chest Cardiac Resuscitation Problems in Training the Laymen in Volunteer Rescue Squads. *New Engl J Med* 272:1, 1965.
4. Cardiopulmonary Resuscitation Techniques, USPHS Symposium Publications 1276, Feb., 1965.
5. Lonn, B., Kleiger, R., Wolff, G.: The Techniques of Cardioversion. *Amer Heart J* 67:282, 1964.
6. Zoll, P. M., Linenthal, A. J.: A.C. and D.C. Countra-Shock for Arrhythmias, *JAMA* 188:327, 1964.
7. Day, H. W.: Effectiveness of an Intensive Coronary Care Area. *Amer J Cardiol* 15:51-54, 1965.
8. Coronary Care Units, USPHS Publications 1250, Oct., 1964.
9. Jude, J. R.: Closed Chest Cardiac Resuscitation — Methods, Indications, Limitation. *Amer Heart Ass Publication*, EM 271 A, June, 1961.
10. Yu, P. N., Fox, S. M., Imboders, C. A., Killip, T.: Coronary Care Units I and II. *Mod Conc Cardiov Dis*, May and June, 1965.
11. Eliot, R. S., Hurwitz, M. M.: Arrhythmias in Acute Myocardial Infarction. *Dis Chest* 45:616, 1964.

Minneapolis Surgical Society

A combined dinner-meeting with the Hennepin County Medical Society will be held March 6, at the Pick-Nicollet Hotel. Dinner at 7:00.

Speaker for the evening will be:

David B. Roos, M.D.
Franklin Medical Center
Denver, Colorado

St. Luke's Hospital Seminar

St. Luke's Hospital, St. Paul, is presenting a seminar entitled "Clinical Aspects of Hematology" on April 27, 1967, starting at 1:30 p.m., in the St. Luke's Hospital auditorium. The featured speaker will be Dr. A. J. Quick of Marquette University Medical School. Contact: C. E. Turbak, M.D. at St. Luke's Hospital.



Meetings and Announcements

Contemporaries appreciate the man rather than the merit; but posterity will regard the merit rather than the man. — Colton

FEBRUARY

- Southwestern Minnesota Medical Society — February 6, Worthington, 7:00 p.m.
 Nicollet-LeSueur County Medical Society — February 6, Holiday House, St. Peter, 6:30 p.m.
 Scott-Carver County Medical Society — February 7.
 St. Louis Co. Med. Society — St. Lukes Hospital, Duluth — February 9, (Ex. Comm. at 6:00 p.m. Regular meeting at 8).
 Minnesota Academy of Medicine — February 8, Town & Country Club, St. Paul, 6:30 p.m.
 Camp Release District Medical Society — February 10, Hunt Hotel, Montevideo.
 Wisconsin Academy of General Practice — February 14-16, Mt. Telemark Ski Conference, Cable, Wisconsin.
 Blue Earth Valley Medical Society — February 15, Interlaken Golf Club, Fairmont.
 Minnesota Academy of Occupational Medicine and Surgery — February 16, Minneapolis Club, 6:30 p.m.
 Twin City Urological Society — February 17, 6:00 p.m.
 Hennepin County Academy of General Practice — February 20, Athletic Club, Minneapolis, 6:00 p.m.
 Ramsey County Medical Society — February 27, 15th floor, Lowry Medical Arts Bldg., St. Paul, 8:00 p.m.
 Postgraduate Course on Leukocytes and the Autonomic Nervous System to be presented prior to the American Academy of Allergy Annual Meeting, February 18-22, at the Holiday Inn-Riviera, Palm Springs, California. Contact: American Academy of Allergy, 756 North Milwaukee, Milwaukee, Wisconsin.
 Sixth National Symposium of the Heart Association of Southeastern Pennsylvania, February 23, at Philadelphia's Sheraton Hotel. Write: Lyle L. Perry, 318 S. 19th Street, Philadelphia.

MARCH

- Northwestern Pediatric Society — March-Spring meeting to be set.

- Zumbro Valley Medical Society — March 1, Mann Hall, Rochester, 8:00 p.m.
 Southwestern Minnesota Medical Society — March 6, Worthington, 7:00 p.m.
 Hennepin County Medical Society and Hennepin County Academy of General Practice — March 6, Pick-Nicollet Hotel, Minneapolis, 6:00 p.m.
 Scott-Carver County Medical Society — March 7, Minnesota Academy of Medicine — March 8, Town & Country Club, St. Paul, 6:30 p.m.
 St. Louis County Medical Society — March 9, Ex. Comm. at 6:00 p.m., regular meeting at 8:00 p.m., St. Mary's Hospital, Duluth.
 Camp Release District Medical Society — March 10, Hunt Hotel, Montevideo.
 Blue Earth Valley Medical Society — March 15, Interlaken Golf Club, Fairmont.
 Twin City Urological Society — March 17, 6:00 p.m.
 Hennepin County Academy of General Practice — March 20, Athletic Club, Minneapolis, 6:00 p.m.
 Ramsey County Medical Society — 8:00 p.m. — March 27, 15th floor, Lowry Medical Arts Bldg., St. Paul.
 Range Medical Society — March 28, Ex. & General Mtg., dinner at 7:00 p.m., Hibbing.
 Area Health Careers Conference for junior, senior high school and college students, El Paso, March 3. Contact: Frank I. Gary, El Paso Public Schools, 1000 West Rio Grande Avenue, El Paso, Texas.

APRIL

- National Methodist Convocation on Medicine and Theology, April 5, 6, 7, in Rochester, Minnesota. Contact: National Methodist Convocation, P.O. Box 102, Rochester, Minnesota 55901.
 Department of Pediatrics at the University of Wisconsin Medical Center, Madison, Wisconsin, will sponsor a three day Postgraduate Conference on "The Mentally Retarded Child," April 6, 7, 8. Contact: Harry A. Waisman, M.D., Joseph P. Kennedy Jr. Laboratory, University of Wisconsin Medical Center, Madison, Wisconsin 53706.

Special Article

Epidemiology of Accident Morbidity

Incidence and A Prevention Program

A. B. ROSENFELD, M.D.*
Minneapolis, Minnesota

A DEATH FROM an accident is as faithfully recorded as is a death from an infectious disease. A case of diphtheria is reported and the statistical data are widely used in the control of epidemics as well as providing a basis for preventive programs. Accidental non-fatal injuries, the chief cause of disability in the age group one to 34 years, are neither reported nor easily available. Thus, little definite epidemiological information exists for community control or prevention programs.

Estimates of the ratio of fatal to non-fatal injuries vary from 100 to 400.^{1,2} Yet most community accident prevention programs are based on mortality data, primarily because this is the only readily available information which can be utilized. Fatalities, however, are a poor index as to the actual extent and nature of accidents which occur over a given period of time within a specified population. Although accidents are the fourth leading cause of death in the general population, they are the leading cause of death in Minnesota of persons under age 35.³ The National Health Survey has shown that the toll from injury—in cost, hospitalization, and suffering—is even more staggering.² National data, however, are not always applicable to local problems. It was therefore decided to survey accidents in Brown County, Minnesota, as a cooperative effort of the State Department of Health and the County Medical Society.

Method

This survey is the first such general county-wide study of non-fatal accidents available in the state. The objectives of the study were to determine the number, type, and cause of medically-attended injuries, to orient community groups as to the nature of the

*Director, Division of Special Services, Minnesota Department of Health, Minneapolis, Minnesota 55440.

Continued

accident prevention problem and to develop effective means of preventing these accidental injuries and deaths. The survey was conducted by sending a checklist, the main items of which are listed in Table 1, to the 22 physicians in the Brown County Medical Society. They were asked to complete the checklist on all patients they examined who had had accidental injuries. The self-mailer checklist was sent to Dr. O. B. Fesenmaier, district health officer in Mankato, for review, and then forwarded to the State Health Department for tabulation and analysis. Two health educators periodically followed up the physician's report by a personal visit. This article covers the first eleven months of the study from October 1, 1962, to August 31, 1963.

Brown County

Brown County is a non-metropolitan area with a total population of 28,542 (1960 census). It contains one city of 11,114 (New Ulm), two towns of 3,492 and 2,701, and a rural population of 10,361. Twenty-two physicians serve the county; thirteen of

them practice in the city. All physicians cooperated in the survey to a greater or lesser extent. One physician filled out only one form; another completed 295 reports. City physicians submitted 87 per cent of all reports.

Reported vs. Expected Injuries

Physicians reported 1,423 injuries during the period of study. It does not appear that they recorded all injuries because of the variable number of cases reported by different physicians and because of low injury rate per capita when compared to the National Health Survey. If the injury rate in Brown County were comparable to the United States rate of 214 accidents per 1,000 persons, about 5,500 injuries should have occurred in the County. Table 2 shows a comparison of the number of reported injuries in Brown County to the number expected from the National Health Survey, varying from a low of 20 per cent in those 65 or older to a high of 34 per cent in the 15 to 24-year-old age group. Although the total reported injuries reached only 26 per cent of the number expected, we think that this first county survey of accidents in Minnesota is worth discussing.

Use of Data

The study was established to investigate how, why, where and to whom accidents occurred and to find means within the community to prevent accidents. After physicians sent in the checklist on patients, the results were summarized in a series of tables (Tables 3-8). The following discussion is based on the data in these tables and on information gathered during follow-up visits by public health educators.

How and Why Accidents Occurred

Knowing how and why accidents occur are the first steps towards prevention.⁴ Falls, cuts, blows, and collisions accounted for 911 or two thirds of 1423 accidents (Table 3). More than one fourth of all accidents resulted from falls, nearly one fifth from cuts, and over one tenth from blows. Only 8 per cent involved car passengers, pedestrians, or

TABLE 1
Accident Injury Report Form
Brown County Accident Survey
October 1, 1962-August 31, 1963

Patient's name, age, sex	Place of occurrence
Marital status	Place of initial treatment
Occupation	Condition of patient
Time of accident	Activity at time of accident
Type of accident	How accident occurred
Nature of injury	Factors contributing to accident
Part of body injured	Preventability

TABLE 2
Reported Injuries by Age Groups Compared With National Health Survey Estimates and Per Cent of Reporting
Brown County Accident Survey
Oct. 1, 1962-Aug. 31, 1963

Age Group	Injuries Reported	Injuries Expected	Per Cent Reported
0-4	191	852	22.4
5-14	280	1,344	20.8
15-24	279	812	34.4
25-44	302	1,107	27.3
45-64	241	1,011	23.8
65+	80	395	20.3
Unknown	50	—	—
Total	1,423	5,521	25.8

ACCIDENT MORBIDITY — ROSENFIELD

cyclists. Physicians had difficulty judging why the accidents occurred and whether they were preventable. They indicated that 47 per cent could have been prevented and that 30 per cent were unavoidable; but in 33 per cent they could not determine the preventability (Table 4).

Where and to Whom

Table 5 summarizes where the accidents took place and what age groups were injured. More than half occurred to persons under the age of 25 years. Close to half of the accidents — 626 out of 1423 — took place in or around the home. Fifty-five per cent of the victims within the home were girls or women, while boys and men suffered 60% of the injuries outside the home. At

work ("Farm Occupational" and "Industrial place or premise"), males over 15 years old made up 83 per cent of all those injured. At play, males were also more susceptible to injury. Eighty-two per cent of persons injured at places of recreation were males, and 64 per cent were less than 25 years old.

TABLE 4
Judgment of Preventability
Brown County Accident Survey
Oct. 1, 1962-Aug. 31, 1963

	Total	Per Cent	Male	Female
Yes	561	39.4	376	185
No	287	20.1	192	95
Can't say	402	28.3	267	135
Maybe	111	7.8	66	45
Unknown	62	4.4	42	20
Total	1,423	100.0	943	480

TABLE 3
Accidents Reported by Type of Accident, Age Group, and Sex
Summary Tables — All Ages
Brown County Accident Survey
Oct. 1, 1962-Aug. 31, 1963

Type of Accident	All Ages			0-4		5-14		15-24		25-44		45-64		65 Years And Over		Age Un- known	
	Total	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Total	1,423	943	480	111	80	202	78	205	74	210	92	151	90	32	48	32	18
Motor Vehicle Driver	42	29	13	—	—	—	—	14	6	11	4	3	2	1	—	—	1
Motor Vehicle Occupant	38	16	22	—	2	3	2	9	7	3	4	—	3	—	1	1	3
Pedestrian	2	2	—	—	—	—	—	—	—	—	—	1	—	1	—	—	—
Cyclist	6	4	2	—	—	3	2	1	—	—	—	—	—	—	—	—	—
Other Bicycle	23	19	4	1	—	15	4	3	—	—	—	—	—	—	—	—	—
Poisoning (Liquid or Solid)	8	5	3	5	3	—	—	—	—	—	—	—	—	—	—	—	—
Poisoning (Gas or Vapor)	3	3	—	—	—	—	—	1	—	1	—	1	—	—	—	—	—
Fall (One Level to Another)	152	85	67	31	16	16	11	10	5	12	8	11	12	4	11	1	4
Fall (Same Level)	222	123	99	26	22	33	16	20	8	11	8	17	22	11	19	5	4
Blow From Object	170	129	41	9	6	28	9	28	6	33	8	21	6	4	4	6	2
Machinery	60	54	6	1	1	2	1	7	—	17	2	23	2	2	—	2	—
Cut by Cutting or Piercing Instrument	147	100	47	6	5	21	6	22	9	28	15	19	10	1	1	3	1
Cut by Other Object	123	78	45	9	5	28	9	13	10	15	14	10	4	—	2	3	1
Fire or Explosion	18	16	2	—	—	—	—	3	1	7	1	5	—	—	—	1	—
Hot Substance	22	10	12	2	4	—	1	2	3	1	2	2	2	1	—	2	—
Firearms	8	8	—	—	—	5	—	—	—	3	—	—	—	—	—	—	—
Foreign Body	58	44	14	4	2	4	1	9	2	16	4	8	3	1	2	2	—
Insect or Reptile	1	1	—	—	—	1	—	—	—	—	—	—	—	—	—	—	—
Animal	51	37	14	5	5	9	2	3	—	8	4	11	3	1	—	—	—
Torsion	63	43	20	—	2	4	2	18	2	17	7	3	6	—	—	1	1
Caught Between 2 Objects	78	42	36	6	2	5	5	6	5	15	5	4	12	3	7	3	—
Collision with Object or Person	97	73	24	2	3	19	7	31	5	9	5	9	2	1	1	2	1
Other	23	16	7	3	2	6	—	2	3	2	1	2	1	1	—	—	—
Unknown	8	6	2	1	—	—	—	3	2	1	—	1	—	—	—	—	—

Continued

Males also predominated in accidents on the street or highway (51 per cent), on sidewalks (58 per cent), and in school or on school grounds (77 per cent). Only in homes, in public buildings, and in the over-65 age group did women have more accidents. Over all, two thirds of those treated for injuries by physicians were males. Preschool children and students were the most susceptible to

injury (Table 6). Among adults, housewives and farmers were most often involved in accidents. Predictably, the safest occupations were those with the least physical activity — professional, managerial, sales, clerical and domestic.

Condition of Patient and Nature of Injury

Physicians reported nine fatalities. Seven males died, six of them over 25 years old (Table 8). Four patients — all males — were totally disabled. But over 92 per cent of the injuries were either non-disabling or only temporarily disabling. The most common types of injuries, in order of frequency, were lacerations and evulsions, which were responsible for almost half of the injuries, contusions and hematomas, strains or sprains, fractures, and burns (Table 7).

Preventive Program

After the data was analyzed, a community program was developed in cooperation with the New Ulm Junior Chamber of Commerce, teachers in the city and county schools, and farm agents and safety groups. The Jaycees started a "home hazard" hunt by giving elementary New Ulm school children a checklist of home safety hazards, the children

TABLE 6
Incidence of Accidents by Occupation
Brown County Accident Survey
Oct. 1, 1962-Aug. 31, 1963

Occupation	Number of Accidents Reported	Per Cent
Student	431	30.3
Preschool	230	16.2
Housewife	196	13.8
Agriculture	167	11.7
Unskilled	109	7.7
Skilled	90	6.3
Semi-skilled	62	4.4
Professional, semi-professional, managerial	50	3.5
Clerical, sales	47	3.3
Service occupations: domestic, personal, building	33	2.3
Other	8	0.5
Total	1,423	100.0

TABLE 5
Accidents Reported by Place of Accident, Age Group, and Sex
Summary Tables — All Ages
Brown County Accident Survey
Oct. 1, 1962-Aug. 31, 1963

Place of Accident	All Ages			0-4		5-14		15-24		25-44		45-64		65 Years And Over		Age Un- known	
	Total	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Total	1,423	943	480	111	80	202	78	205	74	210	92	151	90	32	48	32	18
Home (Indoors)	233	109	124	50	31	26	12	2	13	11	29	5	21	10	16	5	2
Home (Outdoors)	175	92	83	16	29	34	16	9	7	10	6	13	16	7	8	3	1
Farm Home (Indoors)	48	18	30	11	5	3	7	—	2	1	8	2	3	1	5	—	—
Farm Home (Outdoors)	170	115	55	24	9	33	14	12	6	21	14	20	11	2	1	3	—
Farm Occupational	112	103	9	1	—	8	—	11	—	41	4	38	3	2	—	2	2
Industrial Place or Premise	238	203	35	1	—	4	2	53	9	79	11	58	11	1	1	7	1
Place of Recreation	74	61	13	1	1	16	5	31	4	6	2	2	—	—	—	5	1
Street or Highway	133	75	58	1	2	17	9	31	16	20	12	3	12	2	3	1	4
Sidewalk	26	15	11	1	—	6	1	1	—	3	—	2	4	2	4	—	2
School or School Grounds	124	96	28	—	—	43	12	48	10	1	—	3	2	—	2	1	2
Other Public Building	32	15	17	2	—	4	—	—	3	2	5	4	2	2	6	1	1
Other	20	18	2	—	—	3	—	6	1	7	—	1	1	1	—	—	—
Unknown	38	23	15	3	3	5	—	1	3	8	1	—	4	2	2	4	2

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completing the list with the help of their parents. The Jaycees' wives' organization conducted a course in baby sitting and child safety on Saturday mornings with the aid of local police, firemen, and a public health nurse. The Jaycees handed out a pamphlet, "When Teen-agers Babysit," to participants, taught safety techniques, and issued a certificate of completion to those who attended. Literature and a coloring book on poison prevention were distributed to elementary school teachers, to be given to their students for classroom use, along with other brochures on general safety, bicycling, and

swimming. Finally, a plan was worked out with the New Ulm Safety Council to establish a fire prevention program in the schools. This program, not yet in operation, will use fire prevention demonstration kits to illustrate the hazards of electrical, gasoline, gas and rubbish fires.

Summary

The Minnesota Department of Health conducted an eleven-month survey of physician-attended injuries in Brown County, Minnesota, the twenty-two physicians of that county supplying the data on a checklist.

TABLE 7
Accidents Reported by Nature of Injury, Age Group, and Sex
Summary Tables — All Ages
Brown County Accident Survey
Oct. 1, 1962-Aug. 31, 1963

	All Ages			0-4		5-14		15-24		25-44		45-64		65 Years And Over		Age Un- known	
	Total	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Total Accidents Reported	1,423	943	480	111	80	202	78	205	74	210	92	151	90	32	48	32	18
Total Injuries Reported	1,434	949	490	108	88	193	77	220	72	196	93	161	89	35	49	31	22
Laceration or Evulsion	682	460	222	79	52	115	44	79	32	80	42	78	29	13	16	16	7
Contusion or Hematoma	243	156	87	8	4	23	11	41	17	38	17	36	21	5	11	5	6
Sprain or Strain	206	138	68	1	5	25	7	52	14	42	18	10	17	3	3	5	4
Fracture	184	111	73	11	10	22	13	23	3	21	10	22	17	10	16	2	4
Burn or Scald	46	30	16	4	5	1	1	8	5	6	3	7	2	1	—	3	—
Concussion	22	14	8	1	3	2	—	8	—	1	1	2	—	—	3	—	1
Amputation	11	9	2	—	1	2	—	1	—	2	—	4	1	—	—	—	—
Poison	11	7	4	4	4	1	—	—	—	1	—	1	—	—	—	—	—
Asphyxia	3	2	1	—	1	—	—	1	—	1	—	—	—	—	—	—	—
Drowning or Submersion	1	—	1	—	1	—	—	—	—	—	—	—	—	—	—	—	—
Effect of Electricity	1	—	1	—	1	—	—	—	—	—	—	—	—	—	—	—	—
Other	24	17	7	—	1	2	1	7	1	4	2	1	2	3	—	—	—

TABLE 8
Accident Reported by Condition of Patient, Age Group, and Sex
Summary Tables — All Ages
Brown County Accident Survey
Oct. 1, 1962-Aug. 31, 1963

Condition of Patient	All Ages			0-4		5-14		15-24		25-44		45-64		65 Years And Over		Age Un- known	
	Total	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Total	1,423	943	480	111	80	202	78	205	74	210	92	151	90	32	48	32	18
Fatal	9	7	2	—	1	—	—	1	—	3	—	—	—	3	1	—	—
Totally Disabled (Permanent)	4	4	—	—	—	1	—	—	—	—	—	1	—	1	—	1	—
Totally Disabled (Temporary)	83	60	23	2	1	6	—	18	2	11	5	19	3	3	10	1	2
Partially Disabled (Permanent)	5	3	2	—	2	—	—	1	—	—	—	1	—	1	—	—	—
Partially Disabled (Temporary)	503	336	167	16	17	57	25	82	23	98	31	67	45	8	18	8	8
Non-disabled	819	533	286	93	59	138	53	103	49	98	56	63	42	16	19	22	8

Continued

They reported 1423 injuries: nine fatal, 1322 non-disabling or only temporarily disabling. Preschool children, students, housewives, and farmers comprised most of the injured persons, and the majority of their injuries occurred in or near the home. Using this information the members of the Department of Health worked with members of civic organizations, policemen, firemen, and teachers to organize accident prevention programs.

All the physicians participated to a greater or lesser extent. However, this method of gathering data is apparently inefficient as evidenced by the marked variation in individual physician reporting and total report-

ing of only one fourth of the expected number of accidents. Statisticians suggest that a proper sampling, surveyed for a limited time period, can provide more accurate information with less demand on the practicing physician's time and patience.

Acknowledgments

The medical survey was conducted by the District II Health Office in Mankato, O. B. Fesenmaier, M.D., health officer, and the section of public health education, Marie Ford, M.P.H., section chief. Jean Woodbury and Janet Garrison, public health educators, conducted the field work and follow-up. Robert Hiller, chief of section of vital statistics, provided the tabulation and evaluation of the survey. Jerry Sleeper, consultant on accident prevention in the section of maternal and child health, developed and supervised the educational program.

References

1. National Safety Council: Accident Facts, 1966 Edition. National Safety Council, 425 North Michigan Avenue, Chicago, Illinois, 60611.
2. U. S. Department of Health, Education, and Welfare. Public Health Service: Health Statistics from the U. S. National Health Survey, Series B, No. 37. Persons Injured, by Detailed Type and Class of Accident, United States, July 1959-June, 1961. Washington, D. C., Government Printing Office, 1962.
3. Minnesota State Board of Health, Section of Vital Statistics: Vital Statistics, Minnesota, 1964. St. Paul, Minnesota Department of Health, 1965.
4. Rosenfield, A. B., Fesenmaier, O. C., Ford, Marie, Woodbury, Jean, and Garrison, Janet: Medical Reporting of Accidents in a Non-Metropolitan Area, Brown County, Minnesota. Presented at 91st Annual Meeting, American Public Health Association, Kansas City, Mo., November, 1963. Mimeographed copies available from Minnesota Department of Health, Minneapolis, Minn., 55440.

Wisdom Without Vanity

"Medicine," Dr. Tick had confided to flock after flock of students, "is a noble dream and at the same time the most ancient expression of error and idiocy known to man. Solving the mysteries of heaven has not given birth to as many abortive findings as has the quest into the mysteries of the human body. When you think of yourselves as scientists, I want you always to remember everything you learn from me will probably be regarded tomorrow as the naive confusions of a pack of medical aborigines. Despite all our toil and progress, the art of medicine still falls somewhere between trout casting and spook writing.

"There are two handicaps to the practice of medicine. The first is the eternal charlatanism of the patient who is full of fake diseases and phantom agonies. The second is the basic incompetence of the human mind, medical or otherwise, to observe without prejudice, acquire information without becoming too smug to use it intelligently, and most of all, to apply its wisdom without vanity."

— Ben Hecht: Miracle of the Fifteen Murderers.

Conclusion

After thirty years' practice, I am fully convinced that two-thirds of all my patients would have recovered without the use of physic, or the attendance of a physician. — Hufeland (1762-1836) German Physician

Northlands Regional Medical Program

Heart, Cancer and Stroke Law

Public Law 89-239

The Minnesota State Medical Association Foundation has been awarded a planning grant for \$370,904 for the year 1967. Comparable amounts are also made available for the year 1968 and the first half of 1969. The primary objective of the Northlands Regional Medical Program is to assist in providing the best possible medical care in the area of heart, cancer and stroke and related diseases for every resident of the region and thus to attempt to narrow the gap between the least satisfactory and the most satisfactory medical care available in the region. It is planned to accomplish these goals toward improving the overall health of the population without interfering with the pattern or methods of financing of patient care or professional practice or with the administration of hospitals. This will be accomplished with the cooperation of practicing physicians, medical center officials, hospital administrators, the department of health, and representatives from voluntary health agencies.

The following administrative arrangements for Northlands Regional Medical Program have been accomplished:

1. An advisory group has been organized to represent a broad spectrum of interests in the health fields and to represent the public. As the name of the program implies, areas adjacent to Minnesota may wish to be included in the planning. For this reason, representatives from Wisconsin, Iowa, and North Dakota have been included.

2. An executive committee has been formed as a working component of the local advisory group. This committee is made up of members from the two medical centers and from other health agencies in the state. Its members are:

Robert Barr, M.D.
Minnesota State Board of Health
Minneapolis, Minn.

Mr. Harold Brunn
Minnesota State Medical Association
St. Paul, Minn. Secretary Treasurer

Paul Ellwood, M.D.
American Rehabilitation Foundation
Minneapolis, Minn.

Ivan Frantz, M.D.
University of Minnesota
Minneapolis, Minn.

W. F. Mazzitello, M.D.
Minnesota Heart Association
St. Paul, Minn.

Mr. Jack Rivall
Minnesota Hospital Association
Minneapolis, Minn.

Donald Stewart, M.D.
Minnesota Cancer Society
Crookston, Minn.

J. M. Stickney, M.D.
Minnesota State Medical Association
Rochester, Minn.
Program Coordinator

J. P. Whisnant, M.D.
Mayo Clinic
Rochester, Minn.

3. Committees have been designated by the two medical centers to undertake institutional responsibility relating to the Northlands Regional Program.

4. Members of the medical staffs of the University of Minnesota Medical Center and the Mayo Clinic have held meetings with medical and hospital staff personnel at the community level in representative cities throughout the state of Minnesota, Western Wisconsin, and Northern Iowa. In these discussions, it was emphasized that local groups should assist in identifying individual needs with assistance from the regional planning group. As a result of these meetings, planning committees have been formed at the community level in many of the cities visited. These community planning groups will work

Continued

with the medical center staffs and the Regional Medical Program director's office.

5. Contacts have been made with adjoining regions to indicate that the Northlands Regional Medical Program is willing to cooperate in carrying out common programs in overlapping areas.

A number of studies will be undertaken in the early planning stages. The priorities and direction of these studies will be determined by the Northlands Regional Medical Program staff after consultation with the executive committee. Examples of studies are as follows:

1. Identify the resources and capabilities of educational and health service institutions in this region and establish their optimum role in the Regional Medical Program.

2. Determine present grant support and other support in the region for comprehensive health programs other than research project grants.

3. Integrate the efforts of existing medical care programs in regard to state and voluntary health agencies to reduce duplication and promote optimal use of facilities, personnel, and equipment for improved patient care.

4. Determine the existing patterns of patient referral and patient flow to physicians both in outlying regions and to the medical centers.

5. Determine the usefulness of part time educational directors at the community hospital level. Initial efforts will be made in a community and further efforts will be extended from that point.

6. Determine the location of medical and paramedical personnel related to the care of patients with heart disease, cancer, and stroke.

7. Determine the extent to which non-physician personnel could serve in patient care responsibilities and define the training necessary so that such an individual could undertake a role in patient care.

8. Determine the location of physical facilities and services that now exist and that may be necessary for proper diagnosis and treatment of heart disease, cancer, and stroke and consider the proper distribution of

special facilities and equipment in this region.

9. Study the clinical laboratory facilities available to provide diagnostic assistance in regard to heart disease, cancer, and stroke and determine whether regional laboratories would be desirable for special diagnostic tests or whether quality control procedures should be established for hospital or community laboratories.

10. Develop a procedure whereby the quality of medical care can be assessed at various levels of medical practice.

11. Explore more efficient approaches to diagnosis in heart disease, cancer, and stroke such as self-administered questionnaires for history taking and more reliance on routine laboratory procedures to conserve physician time.

12. Investigate the possibility of setting up uniform systems for patient data storage to permit instant retrieval and availability for research and educational purposes.

13. Encourage selected general physicians and internists in some communities to gain additional knowledge in diagnosis and management of either heart disease, cancer, or stroke by spending concentrated periods of time at one of the medical centers, so that such knowledge could be put to use in medical care at the community hospital level.

14. Encourage non-physician personnel to acquire special knowledge by spending concentrated periods of time at one of the medical centers, such knowledge to be put to use in special situations at the community hospital level.

Integration of efforts in continuing education by the medical centers will be an early goal of Northlands Regional Medical Program. The staff for planning and carrying out continuing education at the medical centers should be enlarged and the staff should explore new methods of enhancing continuing medical education. Consideration should be given to self-participation programs in the hospitals, self-teaching video devices, two-way radio communication, one-way telecasting, or two-way television teaching devices.

Identification of existing educational pro-

grams for medical and paramedical personnel that are now provided by voluntary and state health organizations will be necessary. The objectives of individual programs and the origin of the participants will be determined so that these programs can be integrated with other existing and planned programs.

The Northlands Regional Medical Program planning grant will provide funds for the following:

1. Discussions for planning among personnel from the two medical centers, the voluntary health agencies, the State Health Department, the State Hospital Association, the State Medical Association, and community planning groups.

2. Staff for the Northlands Regional Medical Program. Staff to include director and assistant, biostatistician, medical sociologist, research associates and assistants and administrative, secretarial, and clerical staff.

3. Office space for Northlands Regional Medical Program.

4. Support of time for University of Minnesota and Mayo Foundation personnel participating in program development and planning.

5. Clerical assistance for Medical Center planning personnel.

6. Support for medical or paramedical personnel from communities to obtain training in special areas or techniques at either medical center for short periods of time.

7. Support for three half-time area coordinators for education; these individuals to be responsible for assisting in planning continuing education for a community or area in cooperation with one or both medical centers.

Various pilot projects, feasibility studies or operational programs which arise will be evaluated by the executive committee and if approved will be presented to the regional advisory group for approval before submitting an operational grant request to the Division of Regional Medical Programs.

Any interested physician, hospital, or health agency is invited to correspond with the executive committee. Inquiry may be addressed to the Northlands Regional Medical Program, 496 Lowry Medical Arts Building, St. Paul, Minnesota, in care of Mr. Harold Brunn, the Secretary.

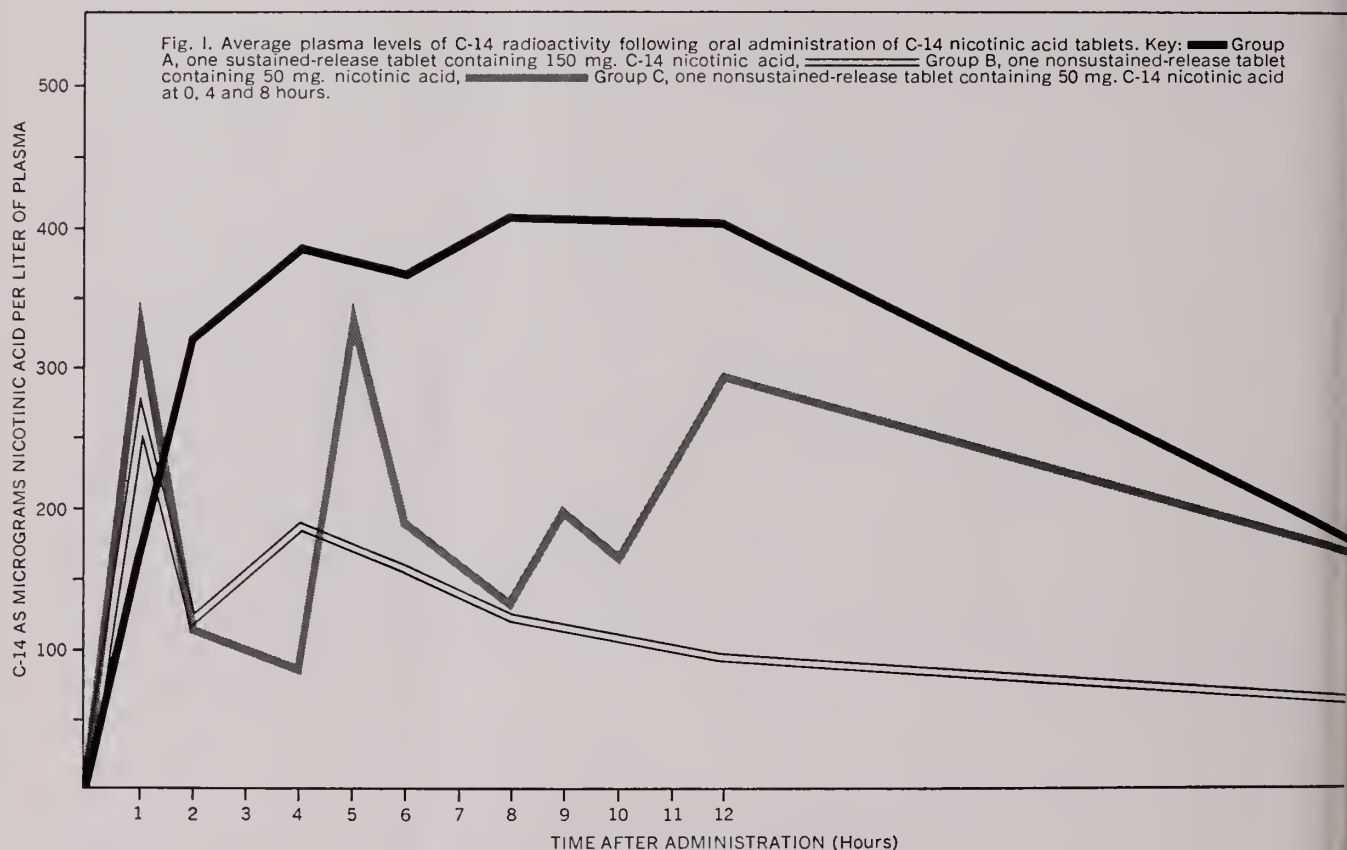
J. M. Stickney, M.D.
Program Coordinator

Importance of Direct Observation

There are several obstacles which have hitherto stood in the way of a more general adoption of the maxim that direct observation constitutes the best method of studying disease. They are the following: the widespread contempt for the authority of the physicians of antiquity; the false opinions and prejudices to which men became attached as if they were idols; the habit of making erroneous comparisons and of drawing hasty conclusions, as well as the formulating of analogies that are based upon untrustworthy reports; reading books which have been unwisely chosen or reading without exercising a discerning judgment; incorrect interpretation of the author's meaning; the craze for reducing everything to a system; and the abandonment, by authors, of the habit of expressing their thoughts in the form of maxims. — Giorgio Baglivi (1669-1707)

There isn't much coasting on the road to success. Success isn't in that direction.
— Williams Laboratory Review

Sustained circulatory, respiratory and cerebral stimulation for the



(fewer absent doses by
absent-minded patients)

Human volunteer subjects were administered Geroniazol TT tablets with the nicotinic acid component made radioactive with C-14. Plasma and urine samples were analyzed. (See Figures I and II) The radioactive tracer study substantiated the previous clinical evidence that the release of nicotinic acid from the Geroniazol TT tablet produced a gradual rise in plasma levels to a plateau for a total of 12 hours and more.

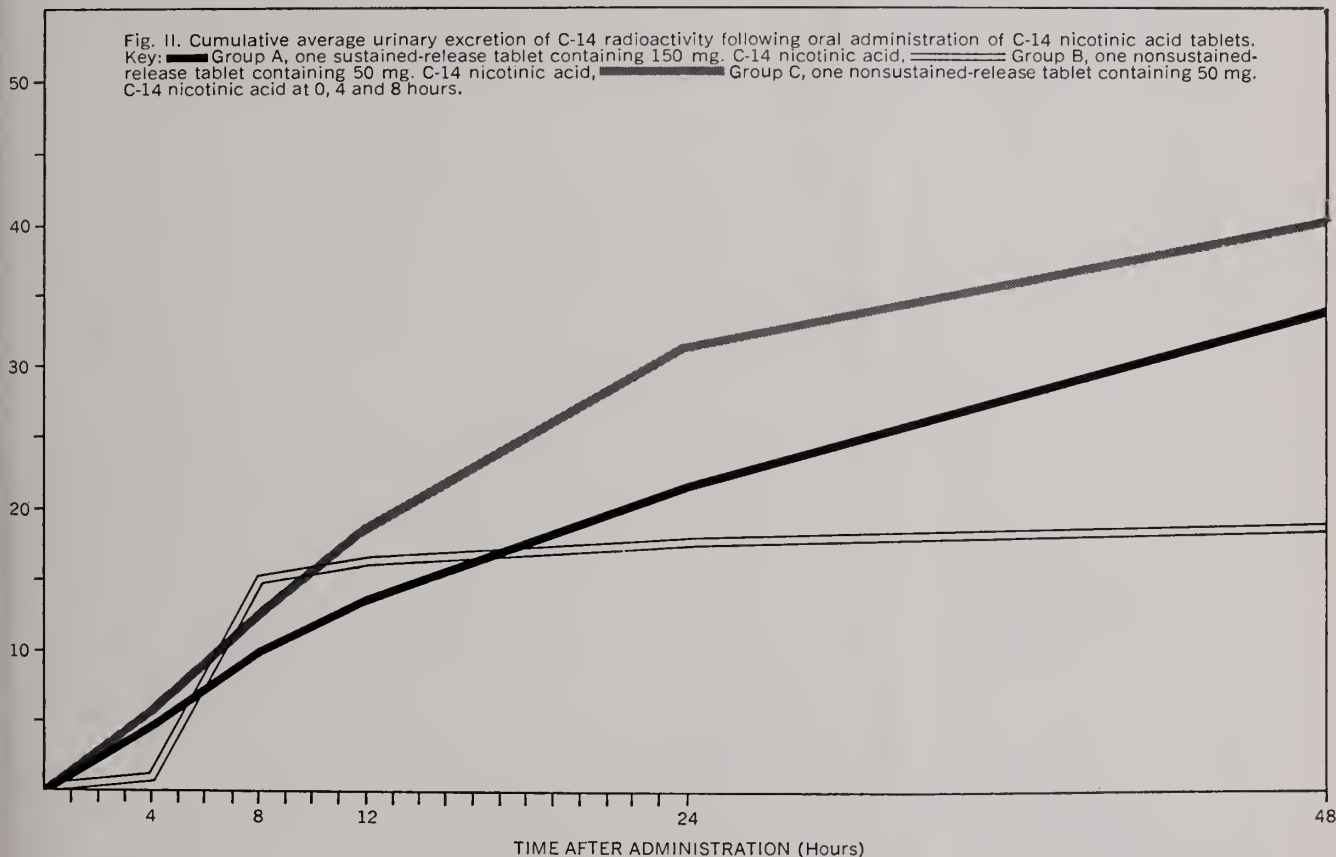
Such proven sustained activity makes the management of geriatric patients much easier by minimizing the possibility of neglected doses through absent-

mindedness or senile confusion. Therapy *can* be continuous on a daily dose of only one Geroniazol TT tablet every 12 hours.

The gradual release of nicotinic acid in Geroniazol TT will provide the well-known peripheral vasodilation needed in patients with deficient circulation and with a minimum amount (if any) of "flushing." Also, cerebrovascular circulation is complemented by pentylenetetrazol, long-established as a cerebral and respiratory stimulant.

Geroniazol TT improves the typical, unfortunate signs of senile confusion. Patients become more alert,

aged and debilitated



ess confused and moody. Personal care, memory, emotional stability, social attention improve. Fatigue, pathy and irritability are reduced.

A prescription for 100 tablets of Geroniazol TT will permit your patients to enjoy the benefits of time-prolonged nicotinic acid/pentylenetetrazol therapy, at an economical price. Dosage is only one tablet every 2 hours.

Contraindications: There are no known contraindications.

Precautions: Exercise caution when treating patients with a low convulsive threshold.

Side Effects: Side effects are rarely encountered, however due to the vasodilatation effect of nicotinic acid, transitory mild nausea, flushing, tingling and pruritus are possible.

Dosage: One tablet every 12 hours.

Supplied: Prescribe bottles of 100 tablets, to take advantage of recent price reduction.

References: 1. Report by Nuclear Science & Engineering Corp., Pittsburgh, Pa., in files of Philips Roxane Laboratories. 2. Connolly, R.: W. Virginia Med. J. 56:263 (Aug.) 1960. 3. Curran, T R., and Phelps, D. K.: Am. Pract. & Digest Treat. 11:617 (July) 1960.



"First with the Retro-Steroids"

PHILIPS ROXANE LABORATORIES

Division of Philips Roxane, Inc., Columbus, Ohio

A Subsidiary of Philips Electronics and Pharmaceutical Industries Corp.

Geroniazol[®] TT

nicotinic acid 150 mg., pentylenetetrazol 300 mg.

Tempotrol[®] Time Controlled Tablet

Norinyl[®] tablets

(norethindrone 2 mg. $\bar{c}$ mestranol 0.1 mg.)

for multiple contraceptive action that has produced a record of unexcelled effectiveness

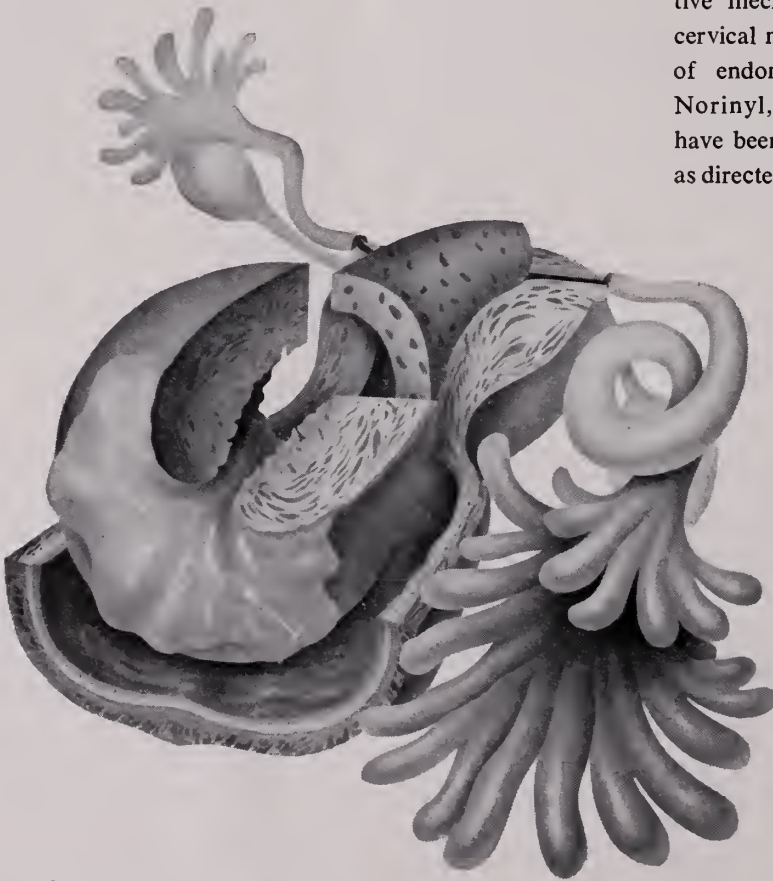
**inhibition of ovulation by means of
2 time-proved hormonal agents**

**production of a cervical mucus hostile to
sperm motility and vitality**

**creation of an endometrium unreceptive
to egg implantation**

no unplanned pregnancies

Norinyl provides multiple action for maximum assurance of success. It does not depend on ovulation inhibition alone for contraceptive effectiveness. The mechanism of action of combined hormonal therapy results in ovulation inhibition reinforced by other protective mechanisms, including a hostile cervical mucus¹⁻¹³ and an acceleration of endometrial changes.^{1-3,7-16} With Norinyl, no unplanned pregnancies have been reported to date when used as directed.



plus important supportive benefits that help her through those critical early months of oral contraception

low incidence of side effects

Low incidence of BTB and spotting, nausea and amenorrhea tends to minimize side effect problems and increases patient cooperation.

no confusion about dosage

An unbreakable "confusionproof" package makes it easy to adhere to prescribed dosage schedule: individually sealed tablets numbered from 1 through 20 *plus* monthly calendar record enables patient to double-check dosage intake by day and corresponding tablet number.



Contraindications: Thrombophlebitis or pulmonary embolism (current or past). Existing evidence does not support a causal relationship between use of Norinyl and development of thromboembolism. While a study which was conducted does not resolve definitively the possible etiologic relationship between progestational agents and intravascular clotting, it tends to con-

firm the findings of the Ad Hoc Advisory Committee appointed by the Food and Drug Administration to review this possibility. Cardiac, renal or hepatic dysfunction. Carcinoma of the breast or genital tract. Patients with a history of psychic depression should be carefully studied and the drug discontinued if depression recurs to marked degree. Patients with a history of cerebral vascular accident.

Warning: Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn.

Precautions: By May 1963, experience with norethindrone 2 mg.—mestranol 0.1 mg. had extended over 24 months. Through miscalculation, omission or error in taking the recommended dosage of Norinyl, pregnancy may result. If regular menses fail to appear and treatment schedule has not been adhered to, or if patient misses two menstrual periods, possibility of pregnancy should be resolved before resuming Norinyl. If pregnancy is established, Norinyl should be discontinued during period of gestation since virilization of the female fetus has been reported with oral use of progestational agents or estrogen. When lactation is desired, withhold Norinyl until nursing needs are established. Existing uterine fibroids may increase in size. In metabolic or endocrine disorders, careful clinical preevaluation is indicated. A few patients without evidence of hyperthyroidism had elevated serum protein-bound iodine levels, which in the light of present knowledge, does not necessarily imply hyperthyroidism. Protein-bound iodine increased following estrogen administration. Bromsulphalein retention has occurred in up to 25% of patients without evidence of hepatic dysfunction. Studies from 24-hour urine collections have shown an increase in aldosterone and 17-

ketosteroids and decrease in 17-hydroxy-corticoid levels. Thus, Norinyl should be discontinued prior to and during thyroid, liver or adrenal function tests. Because progestational agents may cause fluid retention, conditions such as epilepsy, migraine and asthma require careful observation. Thus far no deleterious effect on pituitary, ovarian or adrenal function has been noted; however, long-range possible effect on these and other organs must await more prolonged observation. Norinyl should be used with caution in patients with bone, renal or any disease involving calcium or phosphorus metabolism. **Side Effects:** Intermenstrual bleeding; amenorrhea; symptoms resembling early pregnancy, such as nausea, breast engorgement or enlargement, chloasma and minor degree of fluid retention (if these should occur and patient has not strictly adhered to medication plan, she should be tested for pregnancy); weight gain; subjective complaints such as headache, dizziness, nervousness, irritability; in a few patients libido was increased. In a total of 3,090 patients, 2.2% discontinued medication because of nausea.

NOTE: See sections on contraindications and precautions for possible side effects on other organ systems.

Dosage and Administration: One Norinyl tablet orally for 20 days, commencing on day 5 through and including day 24 of the menstrual cycle. (Day 1 is the first day of menstrual bleeding.)

Availability: Dispensers of 20 and 60 tablets; bottles of 100.

References: 1. Council on Drugs. JAMA 187:664 (Feb. 29) 1964. 2. Bryans, F. E.: Canad Med Ass J 92:287 (Feb. 6) 1965. 3. Goldzieher, J. W.: Med Clin N. Amer 48:529 (Mar.) 1964. 4. Cohen, M. R.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965. 5. Hammond, D. O.: Ibid. 6. Rice-Wray, E., Goldzieher, J. W., and Aranda-Rosell, A.: Fertil Steril 14:402 (Jul.-Aug.) 1963. 7. Goldzieher, J. W., Moses, L. E., and Ellis, L. T.: JAMA 180:359 (May 5) 1962. 8. Kempers, R. O.: GP 29:88 (Jan.) 1964. 9. Tyler, E. T.: JAMA 187:562 (Feb. 22) 1964. 10. Rudel, H. W., Martinez-Manautou, J., and Maqueo-Topete, M.: Fertil Steril 16:158 (Mar.-Apr.) 1965. 11. Flowers, C. E., Jr.: N Carolina Med J 25:139 (Apr.) 1964. 12. Goldzieher, J. W.: Appl Ther 6:503 (June) 1964. 13. The Control of Fertility. Report adopted by the Committee on Human Reproduction of the American Medical Association. JAMA 194:462 (Oct. 25) 1965. 14. Flowers, C. E., Jr.: JAMA 188:1115 (June 29) 1964. 15. Merritt, R. I.: Appl Ther 6:427 (May) 1964. 16. Newland, O. O.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965.

norethindrone—an original steroid from
SYNTEX
LABORATORIES INC., PALO ALTO, CALIF.

Norinyl tablets
(norethindrone 2 mg. • mestranol 0.1 mg.)

for multiple contraceptive action



You can't set her free. But you can help her feel less anxious.

You know this woman.

She's anxious, tense, irritable. She's felt this way for months.

Beset by the seemingly insurmountable problems of raising a young family, and confined to the home most of the time, her symptoms reflect a sense of inadequacy and isolation. Your reassurance and guidance may have helped some, but not enough.

SERAX (oxazepam) cannot change her environment, of course. But it can help relieve anxiety, tension, agitation and irritability, thus strengthening her ability to cope with day-to-day problems. Eventually—as she regains confidence and composure—your counsel may be all the support she needs.

Indicated in anxiety, tension, agitation, irritability, and anxiety associated with depression.

May be used in a broad range of patients, generally with considerable dosage flexibility.

Contraindications: History of previous hypersensitivity to oxazepam. Oxazepam is not indicated in psychoses.

Precautions: Hypotensive reactions are rare, but use with caution where complications could ensue from a fall in blood pressure, especially in the elderly. One patient exhibiting drug dependency by taking a chronic overdose developed upon cessation questionable withdrawal symptoms. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose; excessive prolonged use in susceptible patients (alcoholics, ex-addicts, etc.) may result in dependence or habituation. Reduce dosage gradually after prolonged excessive dosage to avoid possible epileptiform seizures. Caution patients against driving or operating machinery until absence of drowsiness or dizziness is ascertained. Warn patients of possible reduction in alcohol tolerance. Safety for use in pregnancy has not been established.

Not indicated in children under 6 years; absolute dosage for 6 to 12 year-olds not established.

Side Effects: Therapy-interrupting side effects are rare. Transient mild drowsiness is common initially; if persistent, reduce dosage. Dizziness, vertigo and headache have also occurred infrequently; syncope, rarely. Mild paradoxical reactions (excitement, stimulation of affect) are reported in psychiatric patients. Minor diffuse rashes (morbilliform, urticarial and maculopapular) are rare. Nausea, lethargy, edema, slurred speech, tremor and altered libido are rare and generally controllable by dosage reduction. Although rare, leukopenia and hepatic dysfunction including jaundice have been reported during therapy. Periodic blood counts and liver function tests are advised. Ataxia, reported rarely, does not appear related to dose or age.

These side reactions, noted with related compounds, are not yet reported: paradoxical excitation with severe rage reactions, hallucinations, menstrual irregularities, change in EEG pattern, blood dyscrasias (including agranulocytosis), blurred vision, diplopia, incontinence, stupor, disorientation, fever, euphoria and dysmetria.

Availability: Capsules of 10, 15 and 30 mg. oxazepam.

To help you relieve anxiety and tension

Serax[®]
(oxazepam)



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Philadelphia, Pa.

for that added measure of protection

SIGNE M

A 'MAXIMUM SECURITY' ANTIBIOTIC*

*** THE BROAD RANGE DEPENDABILITY OF TETRACYCLINE**

long established as the broad-spectrum agent of first choice in a wide variety of infections

*** WITH THE ADDED SECURITY OF MEDIUM-SPECTRUM REINFORCEMENT**

triacytyleandomycin is highly active against the common 'coccal' pathogens, including certain strains of staphylococci resistant to penicillin and tetracycline

*** ESPECIALLY VALUABLE IN U.R.I.**

provides decisive therapy in acute respiratory infections and other conditions in which staphylococci, streptococci or mixed flora are frequently encountered

*** NOW AVAILABLE IN NEW STRENGTH FOR NEW CONVENIENCE AND ECONOMY**

Signemycin 375 — high-potency capsules for simpler administration, greater patient economy

YCIIN[®] 375

(tetracycline HCl 250 mg.
triacytyleandomycin 125 mg.)

Indications: Indicated in the therapy of acute severe infections caused by susceptible organisms and primarily by bacteria more sensitive to the combination than to either component alone. In any infection in which the patient can be expected to respond to a single antibiotic, the combination is not recommended. Signemycin should not be used where a bacteriologically more effective or less toxic agent is available. *Triacytyleandomycin*, a constituent of Signemycin, has been associated with deleterious changes in liver function. See precautions and adverse reactions.

Contraindications: Contraindicated in individuals who have shown hypersensitivity to any of its components. Not recommended for prophylaxis or in the management of infectious processes which may require more than 10 days of continuous therapy. If clinical judgement dictates therapy for longer periods, serial monitoring of liver function is recommended. Not recommended for subjects who have shown abnormal liver function tests, or hepatotoxic reactions to triacytyleandomycin.

Precautions and Adverse Reactions: *Triacytyleandomycin*, administered to adults in daily oral doses of 1.0 gm. for 10 or more days, may produce hepatic dysfunction and jaundice. Adults requiring 3 gm. of Signemycin initially should have liver function followed carefully and the dosage should be reduced as promptly as possible to the usual recommended range of 1.0 to 2.0 gm. per day. Present clinical experience indicates that the observed changes in liver

function are reversible after discontinuation of the drug.

Use with caution in lower than usual doses in cases with renal impairment to avoid accumulation of tetracycline and possible liver toxicity. If therapy is prolonged under such circumstances, tetracycline serum levels may be advisable. In long term therapy or with intensive treatment or in known or suspected renal dysfunction, periodic laboratory evaluation of the hematopoietic, renal and hepatic systems should be done. Formation of an apparently harmless calcium complex with tetracycline in any bone forming tissue may occur. Use of tetracycline during tooth development (3rd trimester of pregnancy, infancy and early childhood) may cause discoloration of the teeth. Reversible increased intracranial pressure due to an unknown mechanism has been observed occasionally in infants receiving tetracycline. Glossitis, stomatitis, proctitis, nausea, diarrhea, vaginitis and definite allergic reactions occur rarely. Severe anaphylactoid reactions have been reported as due to triacytyleandomycin. Photosensitivity and photoallergic reactions (due to the tetracycline) occur rarely. Medication should be discontinued when evidence of significant adverse side effects or reaction is present. Patients should be carefully observed for evidence of overgrowth of nonsusceptible organisms including fungi, which occurs occasionally, and which indicates this drug should be discontinued and appropriate therapy instituted. Steps should be taken to avoid masking syphilis when treating gonorrhea.



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WANTED: young internist and pediatrician, board certified or eligible, to join five-man group consisting of three GPs, a general surgeon and a radiologist. College town serving population of 22,000 thirty miles from Twin Cities. Salary open with early partnership opportunity. Write or call collect: Ed Jenkins, Manager, River Falls Medical Clinic, River Falls, Wisc. Phone 425-5322.

GENERAL SURGEON — Board certified experienced, all phases surgery and general practice. Prefer Twin Cities area. Write: MINNESOTA MEDICINE — 367; 496 Lowry Medical Arts Building, St. Paul 55102.

WANTED: Young general practitioner to join five-man group consisting of three GPs, a general surgeon, and radiologist. College town serving population of 22,000 30 miles from Twin Cities. Also need LOCUM TENENS in general practice. Contact: Ed Jenkins, Manager, River Falls Medical Clinic, River Falls, Wisconsin, Phone 425-5322.

GENERAL PRACTITIONER wanted to join well-established practitioner. New clinic building — 90 miles east of St. Paul — city of 14,000. Early partnership with full hospital facilities. Ideal location. L. W. Picotte, M.D.; Chippewa Falls, Wisconsin.

FOR SALE: Mattern x-ray unit K.V.-60. Good for chest and extremity work. Also an examining table, instrument cabinet, E.K.G., and other equipment. Contact L. A. Whitesell, Jr., M.D. 207 South 1st Street, Buffalo, Minnesota 55313.

INTERNIST for 20-physician-clinic in prosperous Minnesota city. Salary negotiable first year, then full partnership. East Range Clinic, Virginia, Minnesota.

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OFFICE SPACE now available in busy Bloomington. 713 square feet of new space in building with busy group of G.P.'s, dentist and suburban OB-GYN office. Ideal for ophthalmology, ENT or pediatrics. 8040 Penn Avenue South. 888-9211.

WANTED — Internist, board certified or qualified, to associate with two board certified internists. Ten man multi-specialty group. (Lenont Peterson Clinic, Virginia, Minnesota) — Heart of the expanding taconite industry.

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LARGE GROUP WITH OFFICES IN TWO CITIES is looking for General Practitioner to add to a two-man general practice clinic. Practice limited only by your abilities and interests with ready consultation from specialty partners in other office located in adjacent city. Full partnership after first year. Write: MINNESOTA MEDICINE — 358; 496 Lowry Medical Arts Building, St. Paul, 55102.

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THREE MAN group in North West Wisconsin Resort, State Conservation and Retirement Area needs two more physicians adequately to serve their practice. Facilities offered are three-room physician suites, X-ray and lab under AMT technician, RN-only nursing personnel. New accredited thirty-two bed hospital and forty-six bed nursing home. Deer and duck hunting, fishing within five minutes of town. Internist most needed; generalists welcomed. Will meet any reasonable salary request. Partnership after one year. Write: MINNESOTA MEDICINE — 365; 496 Lowry Medical Arts Building, St. Paul 55102.

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GENERAL PRACTITIONER needed to take over my very active practice on or before June 1, 1967. All equipment nearly new. Records extremely complete. Contact: Gerald E. Cotton, M.D., Fosston, Minnesota.

FOR SALE: Two Hamilton examining tables completely refinished, with treatment cabinet. \$500.00. Call 474-6227, Minneapolis.

GENERAL PRACTITIONER WANTED: To associate with physician-surgeon in Owatonna, a Southern Minnesota community, 25,000 population. Clinic building 3 years old; with five large treatment rooms; lab.; x-ray; central supply; two doctors' offices; pharmacy; and business offices. Located next door to 85 bed City Hospital. Good opportunity for partnership. Contact: O. W. Roberts, M.D.; 920 South Cedar Street, Owatonna, Minnesota. Phone 451-4639.

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\$9,405; \$10,213. Five-year career program \$10,232 to \$18,507. Liberal Civil Service benefits. General practitioners completed internship four years ago may be eligible for NIMH stipends of \$12,000 per year. Write, Director of Education and Research, Northville State Hospital, Northville, Michigan 48167.

GENERAL PRACTITIONER — to join established five-man group consisting of three general practitioners, a general surgeon, and an internist. Excellent clinic facilities situated adjacent to the city hospital. Starting salary negotiable. Retirement plan and many other fringe benefits. Call or write: Richard F. Lehigh, Owatonna Clinic, Owatonna, Minnesota 55060. Phone: 451-1120.

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WANTED — man to fill in two weeks in Feb. or March for general practice in the Twin City Area. Phone — 474-6228 Mpls. Salary open.

EXCELLENT OPPORTUNITY for Intern or Resident finishing in June or July to try practice in Specialty group on locum tenens basis — June 1 thru August 31, 1967. Replacing Internist on leave of absence. Option of remaining on staff if desired. Salary open. Write or call collect, 281-3184, Northwestern Clinic, Crookston, Minnesota.

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A prominent specialist in gastro-intestinal diseases once asked, "How is it possible that you, a general surgeon, see so many of these cases, while I, who am devoting all my time to this work, see so few?" I could only answer, "The thickness of the abdominal wall prevents you from seeing them." — William Mayo



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With Hygroton, you'll discover that you can almost always use fewer tablets than is possible with other diuretics.

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More than any of the newer diuretics, Hygroton brings dosage and cost of medication down to earth.

*Brest, A. N., et al.: J. New Drugs 5:329, 1965.

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chlorthalidone

Indications: Hypertension and many types of edema involving retention of salt and water. **Contraindications:** Hypersensitivity and most cases of severe renal or hepatic disease. **Warning:** With administration of enteric-coated potassium supplements, the possibility of small bowel lesions should be kept in mind. **Precautions:** Reduce dosage of concomitant antihypertensive agents by at least one-half. Discontinue if the BUN rises or liver dysfunction is aggravated. Electrolyte imbalance and potassium depletion may occur; take special care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended. **Side Effects:** Dizziness, weakness, nausea, vomiting, hyperglycemia, hyperuricemia, headache, muscle cramps, postural hypotension, constipation, leukopenia, thrombocytopenia, agranulocytosis, impotence, dysuria, transient myopia, skin reactions, including urticaria and purpura, epigastric pain, or G.I. symptoms after prolonged administration. **Average Dosage:** One tablet (100 mg.) with breakfast daily or every other day. **Availability:** Tablets of 100 mg. in bottles of 100 and 1000. For full details, see the complete prescribing information. 6524-V(B)

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fluocinolone acetonide — an original steroid from

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LABORATORIES INC., PALO ALTO, CALIF.

controls infected inflammatory dermatoses that start from scratch



The "itch-scratch" cycle usually associated with inflammation often results in infected dermatoses because broken skin surfaces are particularly vulnerable to pathogenic bacteria.¹ To treat infected inflammatory dermatoses, Neo-Synalar Cream combines the most active topical corticosteroid with a highly reliable antibiotic generally reserved for topical application.

In Neo-Synalar, fluocinoline acetonide controls the inflammation and provides rapid relief from associated pruritus. At the same time, its antibacterial component—neomycin—combats superficial infection caused by many gram-positive and gram-negative bacilli² that often colonize and thrive on abraded skin.¹

A specially formulated vanishing cream base that is greaseless and odor free makes Neo-Synalar cosmetically appealing, and encourages greater patient cooperation.

controls the infection

stops the scratch

Contraindications: Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of its components. **Precautions:** Neomycin rarely produces allergic reactions. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. **Side Effects:** Side effects are not ordinarily encountered with topical corticosteroids. As with all drugs, however, a few patients may react unfavorably to Neo-Synalar under certain conditions. **Availability:** Neo-Synalar Cream (0.025% fluocinolone acetonide, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes.

References: 1. Pillsbury, D. M., Shelley, W. B., and Kligman, A. M.: A manual of cutaneous medicine, Philadelphia, Saunders, 1961, p. 79. 2. Barber, M., and Garrod, L. P.: Antibiotic and chemotherapy, Baltimore, Williams and Wilkins, 1963, p. 111.

Neo-Synalar[®]

(fluocinolone acetonide-neomycin sulfate cream)

Cream

How long will it take him
to recover from the flu
if he just doesn't care?



Does he really care?
Is he alert, encouraged,
positive and optimistic
about getting out of bed
and back to work soon?

Or is he giving in to
the depressing impact
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When functional fatigue
complicates convalescence,
Alertonic can help...

Pleasant-tasting Alertonic is pipradrol hydrochloride—an effective cerebral stimulant whose gentle analeptic action helps counteract the apathy and inertia that so often delay convalescence—together with an excellent vitamin and mineral formula, in a satisfying 15% alcohol vehicle.

Nothing fosters confidence and a sense of well-being better than your own personal warmth, understanding and encouragement together with Alertonic to help insure prompt response.

*Adequate dosage is important: Prescribe Alertonic—
one tablespoonful t.i.d., 30 minutes before
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**Os
frontale**

**Sinus
frontalis**

**Crista
galli**

**Os
nasale**

Lamina cribrosa ossis ethmoidalis

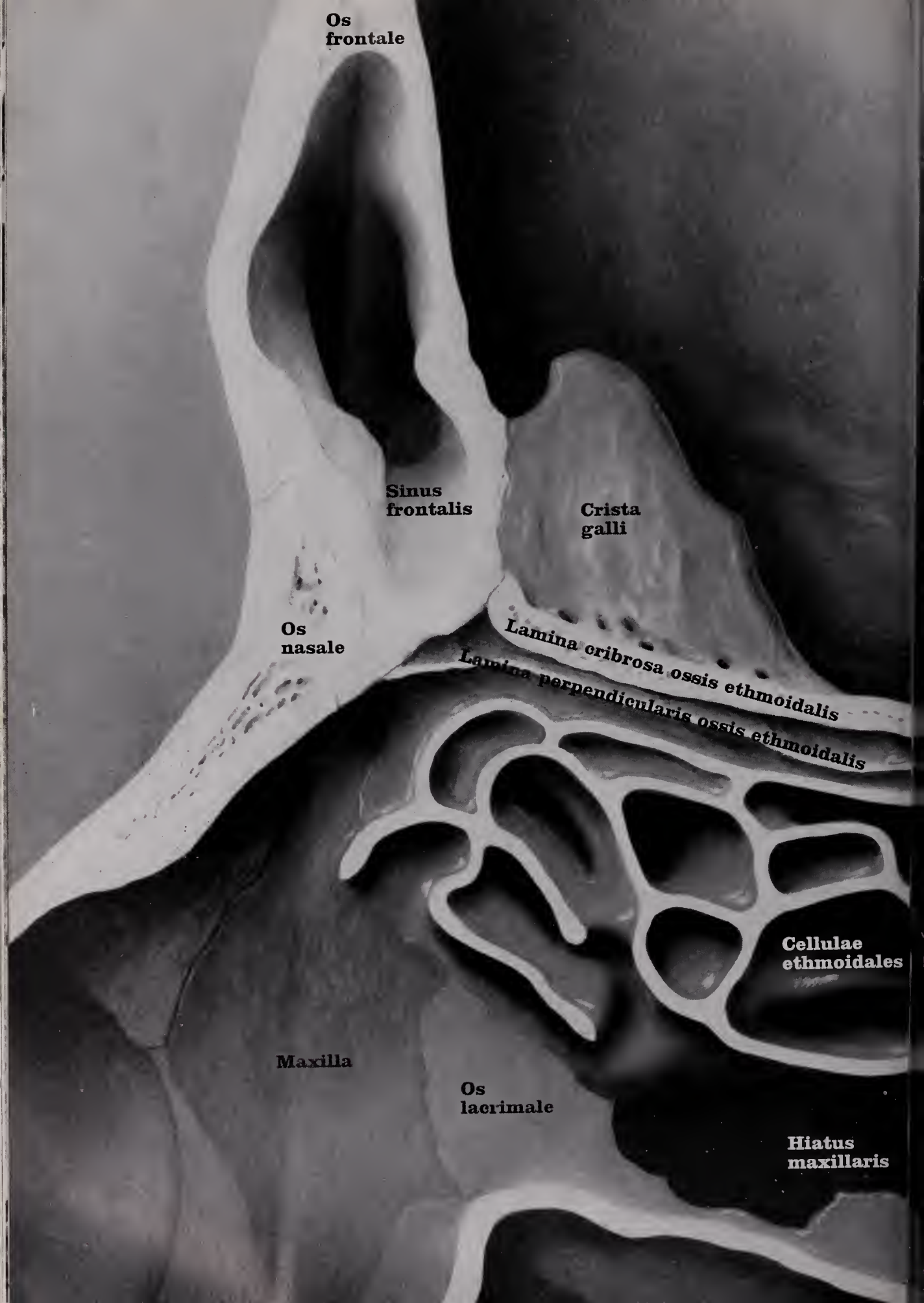
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**Os
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B

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Contraindications: History of sensitivity or severe intolerance to aspirin or meprobamate.

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Saxon

Minnesota Medicine at a Glance

Carcinoma of the Pancreas and the Ampulla of Vater — Sako Page 169

Early carcinoma of the pancreas is difficult to detect clinically. By the time the commonly recognized symptoms and findings occur, over three fourths of the patients have passed the stage where resection is possible. However, definite progress, though painfully slow, has been made over the past thirty years, as reflected in the continued decline in operative mortality, and also in a five-year-survival rate as high as 14% at the hands of some operators with extensive experience in surgery of the pancreas.

Management of Head Injuries — Wilson and Norrell Page 177

Most patients with acute head injuries can be successfully treated at the average general hospital without neurosurgical consultation. Close observation of the patient is essential. A baseline in the patient's general condition and neurological signs must be established and all changes promptly noted. Except for extradural hemorrhage, head injuries usually do not constitute surgical emergency; and other serious injuries may take precedence. Head injury alone rarely produces shock. In the comatose patient tracheostomy is necessary to maintain a free airway, and nasogastric suction to prevent aspiration. A urinary catheter will elicit genitourinary injury and also aid in assaying fluid balance by monitoring the patient's output. Bradycardia, a rise in systolic blood pressure, and slowing of the respiratory rate signify increased intracranial pressure and require immediate consultation. Extradural hemorrhage requires emergency evacuation of the hematoma and may have to be done by any surgeon available without special equipment. A technique is presented.

Retrograde Arteriography — Sweet and Grismer Page 185

Sweet and Grismer have found the percutaneous non-catheter retrograde brachial arteriography to be entirely safe and reliable for the purpose of demonstrating the abnormalities in the vertebral vessels. They have used it in 55 studies with no adverse effects. The details of the technique are well described in their manuscript.

Addiction — Koutsky and Larson Page 189

Addiction to drugs and alcohol was the major problem in 7.5 per cent of the patients admitted to a general hospital psychiatric service. Minor tranquilizers and non-barbiturate sedatives are of major importance in the problem. Addiction is easily overlooked in patients with better social adjustment or in those with medical or surgical complaints. Addiction occurs in people of all social classes whether of rural or metropolitan origin. Seventy-four per cent of these patients showed significant problems with depression or character disorders. Deaths have been reported following the withdrawal of barbiturates, meprobamate, and methypylon. Grand-mal convulsions, hyperpyrexia, and delirium are symptoms of impending disaster. The authors discuss the effects of abrupt withdrawal versus gradual withdrawal of these medications and recommend the grad-

ual withdrawal of the drug of addiction to avoid complications. Although their data is too limited to make a definite statement, they suggest the use of anti-convulsants during withdrawal. They feel that phenothiazine drugs are safe to use during withdrawal provided anticonvulsant treatment is given concomitantly. They urge further study of the effectiveness of anti-seizure medication during withdrawal. They comment on the serious difficulty in achieving satisfactory follow-up care for the chronic addict.

Wringer Injuries — Garrick

Page 195

With the advent of the automatic clothes washing machine, wringer injuries are now seen much less frequently by physicians. Nonetheless, their severity should not be underestimated. The extent of damage to crushed tissues cannot be accurately assayed at the original examination. The physician who initially examines and treats the injury should not make the error of undertreatment just because there are minimal superficial signs of injury. The first treatment should consist of a gentle, thorough, aseptic cleansing of the involved extremity, suture of lacerations, followed by a carefully applied massive compression dressing. Tetanus prophylaxis should be given. Further treatment depends on the condition of the tissues at subsequent dressings in the next few days.

Gastrointestinal Bleeding Caused by Aortojejunal Fistulization — Larson et al.

Page 203

Aortoenteric fistula is a surgical emergency which must be suspected in any patient with gastrointestinal bleeding who has had a previous abdominal aortic graft. The faulty graft must be exposed and completely removed at the time of reconstruction. This complication can be prevented at the primary procedure by meticulous construction of the aortic anastomoses, avoidance of a discrepancy in the size of the host aorta and the graft, avoidance of injury to the bowel wall, and interposition of viable tissue between the graft and the bowel.

Hereditary Hemorrhagic Telangiectasia — DeSanto

Page 233

Telangiectasia of the skin with hemorrhage, often nose bleed, and a history of hemorrhage in the family represent the triad known as Rendu-Osler-Weber disease. Many methods of treatment have been tried and many complications from treatment have resulted. Therapy should involve the least drastic procedure necessary to control the symptoms. Iron replacement and transfusions, often many transfusions, are necessary.

Intuition

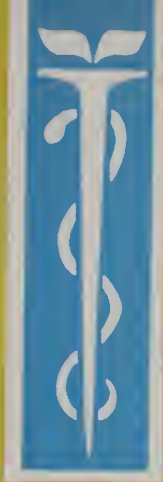
Perhaps the ability not only to acquire the confidence of the patient, but to deserve it, to see what the patient desires and needs, comes through the sixth sense we call intuition, which in turn comes from wide experience and deep sympathy for and devotion to the patient, giving to the possessor remarkable ability to achieve results. — William Mayo

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D. D. Etzwiler, M.D.

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MARCH, 1967

vol. 50 #3

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(1) Portnoy, J.; Brewer, J. and Harris, A.: PUBLIC HEALTH REPORTS, 77:645-652, August 1962. (2) Joseph, J. M. and Warner, G. S.: A WORKSHOP MANUAL. Md. State Dept. Health, Bureau of Lab., Balto., Md., September 1962. (3) Wollenweber, H. L.: OFF. PATH., 2, February 5, 1963. (4) Portnoy, J.: MILIT. MED., 128:414-417, May 1963. (5) Portnoy J.: THE AMER. JOUR. OF CLIN. PATH., 40:473-479, November 1963. (6) Buck, A. A. and Mayer, H.: THE AMER. JOUR. OF HYG., 80:85-90, July 1964. (7) Brown, W. J.; Donohue, J. F. and Price, E. V.: PUBLIC HEALTH REPORTS, 79:496-500, June 1964. (8) Clayton, J. L.; Lindhardt, E. M. and Fraser, R. S.: PUBLIC HEALTH LAB., 22:206-207, November 1964. (9) Luca-torto, F. M.; Katz, B. D. and Toto, P. D.: THE J.A.D.A., 69:697-699, December 1964. (10) Portnoy, J.: PUBLIC HEALTH LAB., 23:43, March 1965. (11) Reed, E. L.: PUBLIC HEALTH LAB., 23:96-103, May 1965.



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D. D. Etzwiler, M.D.

St. Louis Park, Minnesota

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References: 1. Batterman, R. C., and Grossman, A. J.: *Fed. Proc.* 14:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: *The Pharmacological Basis of Therapeutics*, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Roth, J. L. A., et al.: *Gastroenterology* 44:146, 1963. 4. Conney, A. H., and Burns, J. J.: *J. Pharmacol. Exp. Ther.* 123:340, 1960. 5. Settel, E.: *Clin. Med.* 6:1373, 1959. 6. Berman, H. H., et al.: *Dis. Nerv. Syst.* 25:430, 1964. 7. Darienzo, C.: *Ibid.*, 27:189, 1966.

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President's Letter

IF THE SOCIAL planners have their way and — make no mistake — they are a powerful and effective group in this country, we have acquired an illuminating glimpse into some of their ideas at a recent hearing before the Minnesota State Legislature House Committee on Appropriations. Mr. Fitzsimmons, as well as the other members of his committee who were present, may not have liked what they heard any better than I did.

We heard testimony from many people that day regarding "Medical Manpower." One of the principal physicians to give testimony was Osler L. Peterson, M.D., of Harvard University, Executive Director of the "Health Manpower for the Upper Midwest" study, requested by the University of Minnesota Board of Regents, and financed by the Louis W. and Maud Hill Family Foundation of St. Paul. This report is well worth study by each physician in our Midwest and North Central area.

In this letter I shall comment on one small, but important part of his testimony. He stated that "transportation will have to take the place of specific services." With this we can all agree. With the dwindling supply of physicians in rural America, Dr. Peterson urged that we should consider doing what most of the European countries have done, namely, make much more use of paramedical personnel for as many services as possible, in order to free the physician for more technical work. Among those suggested was an almost vanished person, at least in this area, the "midwife."

Dr. Peterson asked (to paraphrase him): "If England, as well as other European countries can use their services, why not

America?" I would like to pose this question: Just because these other countries use midwives to replace physicians in the prenatal, natal, and postnatal periods, does this mean that this is good? In my opinion this step would be retrogressive. Unfortunately, "it could happen here." All who have studied the subject agree that it will take many years before enough physicians are graduated to meet the needs. These studies show that, if expansion could start immediately, it would still be at least 1975 before more physicians could be made available.

We would hope that an adequate number of these future physicians and, indeed, of our presently graduating young men and women, might choose to begin to fill the vacancies in rural areas. We don't want this done by legislation, but that could happen too.

An equally urgent, and even more disturbing problem, in this writer's opinion, is the need for redefinition of the term "General Practitioner." The search goes on, and will be the subject of a future letter.

With the rapidly expanding population, plus stepped-up research in all fields, diabetes continues to tantalize the best judgment which any physician can offer to his own group of patients with this disease. This issue is devoted especially to newer thoughts on this important subject, and we recommend it for your study.

C. G. Sheppard, M.D.

C. G. Sheppard, M.D.
President
Minnesota State Medical Association

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Diabetes Mellitus

Outline of Methods for Early Diagnosis

GEORGE D. MOLNAR, M.D.*
VAHAB FATOURECHI, M.D.**
FREDERICK J. SERVICE, M.D.**
Rochester, Minnesota

SYMPTOMATIC DIABETES mellitus is usually easy to diagnose. Clinically latent, earlier stages of diabetes are not. Application of recently acquired knowledge in this field permits ever earlier diagnosis, if the proper tests are correctly applied. A brief survey of this vast and fast-growing segment of the literature on diabetes is the purpose of this communication.

Diabetes mellitus can be defined as the abnormal metabolic state related to deficient insulin activity. This deficiency refers not only to the level of circulating insulin, which may actually be low, normal, or high,¹ but also to the effectiveness of endogenous insulin, which in turn is customarily gauged by tests of glucose tolerance. However, impaired carbohydrate metabolism is not necessarily synonymous with diabetes, since a host of conditions such as myocardial infarction, severe burns, blood dyscrasias,² and some endocrine disorders may also impair carbohydrate tolerance. Although carbohydrate metabolism is certainly *not all* that is disturbed in diabetes, traditionally, when doubt exists, tests of glucose tolerance are still the standards whereby diagnostic decisions are reached.

Screening Tests

Screening tests for diabetes (Table 1) include urinalysis and fasting or postprandial blood-sugar determination. The urine specimen examined can be a single voiding or a prolonged collection. The analysis can be qualitative or quantitative³ and specific for glucose³ or simply a measurement of reducing substances. The subject can be in the fasting or postprandial state. The load of carbohydrate, if one is administered, can be measured or unmeasured. The individual may be free from or

*Mayo Clinic and Mayo Foundation: Section of Medicine.

**Mayo Graduate School of Medicine (University of Minnesota), Rochester: Residents in Medicine.

under spontaneous or deliberate stress in terms of the absence or presence of illness other than diabetes or through the administration of adrenocortical steroids. Obviously, all of the foregoing considerations affect the relative diagnostic value of urinalysis as a screening procedure for diabetes.

For blood tests used in screening for diabetes (Table 1), the specimen can be venous or capillary or arterial, whole blood or plasma, and the analysis can be specific for glucose or not, and performed manually or by automation.⁴ More important, how-

ever, is specifically whether the subject is in the fasting or postprandial state.

Fasting Blood Sugar

When the fasting concentration of blood glucose is significantly increased, repeatedly and under acceptable conditions, the diagnosis may be made and tests of tolerance omitted. Obtaining a fasting specimen has the advantage of being easily standardized, as it is easy to instruct a patient not to eat after the evening meal the night before the test. For the early detection of diabetes, however, the fasting blood-glucose measurement is insensitive.⁵

Postprandial Blood Sugar

A postprandial specimen for blood-glucose determination with a timed sampling procedure after a measured load can be useful for early diabetes detection, but a randomly collected specimen following an unmeasured load has been shown to be just as inefficient as the fasting blood-glucose determination for the same purpose.⁶ About 30% of very early cases will be missed.⁶ If a measured load is used, its magnitude can be of considerable importance.

As will be mentioned later with reference to tolerance tests, the subject's preparation for an isolated blood test is also of importance.

Tolerance Tests

The considerable variety of tolerance tests, in all of which changes in blood-glucose concentration are measured, is indicated in Table 2.

Oral Tolerance Test

Among oral tolerance tests, food or glucose can be the load. Doses of carbohydrate given range between 50 and 100 gm. The glucose load, if one is calculated, ranges from 0.5 to 3 gm./kg. of body weight; but this may also be calculated on the basis of kilograms to the 0.7 power⁷ or be suitably adjusted to body surface area. Furthermore, actual or ideal weight or surface area may be used in such calculations (Table 2). The duration of the test is two to five hours

TABLE 1
Screening Tests

Urinalysis	
Specimen:	Single voiding or prolonged collection
Analysis:	Qualitative or quantitative ³ Reducing substances or glucose ³
Subject:	Fasting or postprandial Measured or unmeasured load Stressed or unstressed
Blood test	
Specimen:	Venous or arterial Whole blood or plasma
Analysis:	Reducing substances or glucose Manual or automated
Subject:	Fasting Postprandial Random or timed sampling Measured or unmeasured load Magnitude of load Preparation

TABLE 2
Diagnostic Tests Measuring Blood Sugar

Glucose tolerance	
Oral (food or glucose)	
Load: Fixed dose, e.g., 50-100 gm.	} Actual or ideal body size
Calculated dose, e.g., 0.5-1.75-3 gm./kg. (or /kg. ^{0.7})	
or	
Calculated dose adjusted to surface area	
Duration: 2-5 hr.	
Sampling: Half-hourly; hourly; continuously	
Intravenous (rapid or slow)	
Load: 25-30-50 gm.	
0.25-3 gm./kg. etc.	
Duration: 1-3 hr.	
Sampling: 15 minutes; half-hourly; continuously	
Cortisone-glucose tolerance; insulin-glucose tolerance; tolbutamide tolerance; glucagon-glucose-tolbutamide tolerance	

and the sampling can proceed half-hourly, hourly, or on a continuous automatic recording basis.⁴

Intravenous Tolerance Test

The intravenously administered load of glucose can be given rapidly, that is, usually in about three to five minutes, or slowly throughout an hour. The loads range from 0.25 to 3 gm/kg.,⁷ and again the various considerations cited previously for body size may be taken into account. The usual dose is 25 to 50 gm., the duration of the test is one to three hours, and sampling can be done every 15 or 30 minutes or continuously.

Cortisone-Glucose Tolerance Test

Further refinements of load tolerance testing involve varieties of the cortisone-glucose tolerance test. This now is the prototype of a test designed to detect an earlier stage of diabetes.⁸ The glucose load is administered during the effect of a previously given adrenal corticosteroid. A good indication for the use of cortisone-glucose tolerance tests is in kinship surveys of diabetic patients to diagnose prediabetes.^{8,9}

Insulin-Glucose Tolerance Test

The insulin-glucose tolerance test involves the administration of insulin in conjunction with a load of glucose. Indications for this test are suspected impairment of either insulin responsiveness or carbohydrate tolerance or of both. Impairment of insulin responsiveness seems to be an important phase in the pathogenesis of diabetes.¹⁰

Tolbutamide Tolerance Test

The tolbutamide tolerance test measures insulin secretory capacity of the pancreatic islets. It differs from the other tolerance tests by employing a noncarbohydrate load. Even more intensive stimulation of insulin secretion may be obtained through combined administration of glucagon, tolbutamide, and glucose.¹¹

Preparation and General Condition of Subject

An important aspect of all the tests is

preparation of the subject. If the test is done on an unprepared subject, carbohydrate intolerance may be observed because of starvation in a normal individual, perhaps through the mechanism of enhanced secretion of growth hormone.¹² In a mildly diabetic subject, abstinence from carbohydrate consumption or starvation may ameliorate the tolerance test to the point of a normal response through improved ability to secrete insulin.¹³ Dietary preparation also helps to standardize a test so that repetitions may yield essentially similar responses.

The Influence of Calories

Wilkerson and associates¹⁴ have shown that, with a calorically adequate diet, carbohydrates might be restricted to less than 50 gm/day before abnormalities show up, but even they recommend dietary preparation with 150 to 200 gm. of carbohydrate for at least three days.¹⁴ Others recommend a level of 300 gm.¹⁴ With an average North American diet, fat and protein content of the dietary preparation need not be especially emphasized, though generally it is important. Thus the matter of the total calories consumed prior to the test is important, and even eating habits matter: nibbling of food favors and gorging impairs carbohydrate tolerance.¹⁵

Influence of Exercise and Drugs

Lack of exercise prior to the test, such as confinement to bed for some time, may impair carbohydrate tolerance, whereas exercise during the test improves it, especially in the mild diabetic.¹⁶ Supine position delays gastric emptying and alters glucose absorption.¹⁷ The oral glucose tolerance test is best done with the patient in the sitting position. Drugs being used by the patient such as corticosteroids,¹⁸ sex steroids¹⁹ (oral contraceptives),²⁰ and thiazides are known to affect carbohydrate tolerance. The patient must be questioned in this regard.

Influence of Age and Disease

Age and state of health are other factors to be considered (Table 3). It is increasingly

well documented that age from childhood through adolescence to old age brings with it progressive impairment of carbohydrate tolerance.²¹ It may be justifiable to adjust diagnostic criteria for diabetes according to age.²¹ Pregnancy, endocrine diseases, other diseases, and major stresses may have adverse effects on carbohydrate tolerance. In general, it is justifiable to make a working diagnosis of diabetes in the presence of another illness, but it is important that re-testing be undertaken when the patient is fully treated or cured.

Diagnostic Criteria

The diagnostic criteria depend on a laboratory's normal range. Decisions based on a single abnormal point are unjustified. In the oral glucose tolerance test the two-hour value may nevertheless be the most impor-

tant single value. A value of 110 mg./100 ml. by a so-called true blood-sugar method is considered abnormal.²² The one-hour value may be the next most important; values above 150 mg. may be abnormal. When available, the 30- and 90-minute values can help resolve an otherwise borderline result. The fasting value should not exceed the normal range for the particular laboratory. The three-hour value likewise should be back to the normal (fasting) range, and if hypoglycemia is present, this, too, can be of diagnostic significance. Ninety minutes after an intravenous load of glucose, values in the normal fasting range are expected. Calculations of a K-value, or rate of glucose utilization, the slope of glucose disappearance, and the glucose-disposal rate have advantages in yielding a single number to describe the organism's response to the glucose load.⁷

TABLE 3

Factors in Patient's General Condition to Be Considered

Age
Pregnancy
Endocrine disease
Pituitary
Adrenal
Thyroid
Other diseases
Hepatic
Gout
Neoplasia
Acute illness
Major stress
Emotional
Traumatic, etc.

TABLE 4

Diagnostic Tests Measuring Additional Parameters During or With Glucose Tolerance Test

Insulin
Immunoreactive
Normal range fasting and at 150 min.
Three- to 10-fold increase in 30-60 min.
High or low values, delayed or no rise in diabetes
Insulin-like activity
Muscle
Fat
Other hormones: growth hormone, glucagon, etc.
Free fatty acids, ketone bodies
Phosphorus, electrolytes
Intermediary metabolites
Carbohydrate
Fat
Protein
Tissue biopsy
In-vivo examination of bulbar conjunctiva

} For presence of
microangiopathy,
tissue changes, etc.

Additional Diagnostic Methods

Measurement of substances other than glucose (Table 4) during a glucose tolerance test provides means of detecting diabetes especially in early, prediabetic, or borderline conditions.

Plasma Insulin

Important recent progress has provided radioimmunoassay and bioassay methods for determining plasma insulin. Normal fasting values for plasma insulin vary with the method of determination. After an oral glucose load, peak values for insulin are reached in 30 to 60 minutes. These are usually three to 10 times the fasting value^{1,23,24} and return to fasting level in 120 minutes.²³ During the intravenous glucose tolerance test, the plasma-insulin response is significantly lower and less sustained.²⁵

In mild maturity-onset diabetes a delayed but exaggerated insulin secretory response to glucose loading may occur.¹ In contrast, very low or no insulinogenic reserve is the rule in juvenile-onset diabetes.¹

Serum Free Fatty Acids

Other parameters listed in Table 4 can be measured during tolerance tests. How-

ever, a number of these at present have limited application and as diagnostic aids are still controversial. For instance, in a diabetes survey, although fasting free fatty acid levels in the group with impaired but not fully abnormal carbohydrate tolerance were elevated in 30%, there was also a wide scatter of values in normal subjects.²⁴ Elevated fasting levels of free fatty acids are a frequent finding in diabetes, and indeed elevated free fatty acid levels have been incriminated in the impairment of glucose tolerance.^{26,27} Shafrir and Gutman's response curves obtained during oral glucose tolerance tests showed that 50% of those suspected of having diabetes had distinctly abnormal free fatty acid values similar to those obtained from diabetics.²⁸ However, the finding that 40% of the non-insulin-dependent proven diabetics gave normal free fatty acid responses raises serious doubts about the diagnostic usefulness of this parameter. Abnormal free fatty acid-response curves have also been observed²⁹ during rapid intravenous glucose tolerance tests in subjects genetically predisposed to diabetes, in contrast to normal responses in normal subjects.

In relatives of diabetic patients, in whom blood-glucose and free fatty acid values were normal during oral glucose tolerance tests, the cortisone-glucose tolerance test yielded borderline glucose values and also distinctly abnormal free fatty acid response curves during the latter test.³⁰ These data support the thesis that free fatty acid measurements may disclose the first detectable abnormalities in individuals genetically predisposed to diabetes.²⁹

Hypertriglyceridemia

Impaired carbohydrate tolerance has been recognized in hypertriglyceridemia by use of oral and intravenous glucose tolerance tests measuring glucose and free fatty acids.³¹ The usefulness of determining fasting triglyceride levels as an aid to diagnosis in early or borderline cases, however, is hampered by the fact that 30 to 40% of the normal population have some degree of hypertriglyceridemia.

Microangiopathy

When biochemical changes in body fluids are still normal or borderline, light and electron microscopic studies of tissue biopsy specimens from renal and other tissues for microangiopathy and from skin for elastic-tissue changes, and in-vivo observations on the microcirculation of the bulbar conjunctiva show great promise³² for early detection of diabetes. This approach has the advantage of independence from biochemical diagnostic methods.

Summary

Methods of diagnosing diabetes mellitus have been outlined with emphasis on detection of early phases of the disease. In borderline cases, tests of glucose tolerance alone or in combination with biochemical determination other than blood-glucose measurement or in combination with tissue diagnostic methods will often, but not invariably, resolve the diagnostic dilemma. The importance of proper preparation of the subject and consideration of his general condition when he is being tested for diabetes must not be neglected.

References

1. Berson, S. A., and Yalow, Rosalyn S.: Some Current Controversies in Diabetes Research. *Diabetes*. 14:549, 1965.
2. Lisker, S. A., Brody, J. I., and Beizer, L. H.: Abnormal Carbohydrate Metabolism in Patients With Malignant Blood Dyscrasias. *Amer J Med Sci* 252:282, 1966.
3. Fine, J.: Glucose Content of Normal Urine. *Brit Med J* 1:1209, 1965.
4. Burns, T. W., Bregant, R., Van Peenan, H. J., and Hood, T. E.: Observations on Blood Glucose Concentration of Human Subjects During Continuous Sampling. *Diabetes*. 14:186, 1965.
5. Hainline, A., Jr., and Keller, D. F.: An Evaluation of the Fasting Blood-Glucose Level as an Index of Abnormal Carbohydrate Tolerance. *Cleveland Clin Quart* 31:209, 1964.
- 6-32 May be secured from the author or the reprints.

Love may be blind, but marriage is an optometrist. — Banking

IT'S THE LAW

Live Birth Defined

1. Statutory Provision

"Live Birth" means the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy, which, after such separation, breathes or shows any other evidence of life such as beating of the heart, pulsation of the umbilical cord or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached; each product of such a birth is considered live born. (Section 144.151, Minnesota Statutes Annotated through 1964 Supplement)

Fetal Death Defined

1. Statutory Provision

"Fetal death" or "stillbirth" shall have such meaning, in terms of the duration of pregnancy, as the State Board of Health may from time to time by regulation ascribe to such words. (Section 144.151, Minnesota Statutes Annotated through 1964 Supplement)

2. Regulation

Fetal death is death prior to the complete expulsion or extraction from its mother of a product of conception after twenty weeks of gestation. The death is indicated by the fact that after such separation the fetus does not breathe or show any other evidence of life such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles. (Regulation 126, Minnesota State Board of Health, effective March 9, 1956)

When Fetal Death Registration Is Required

From the definition set forth above, fetal death registration is required if the 20th week of gestation has been completed.

1. Statutory Provision

A certificate of every . . . stillbirth shall be filed . . . within five days . . . with the local registrar. (Section 144.163, Minnesota Statutes Annotated through 1964 Supplement)

Medical Men on Postage Stamps*

Charles Nicolle (1866-1936), Nobel Prize winner in 1928, was a French physician who did valuable research in rinderpest,** measles, diphtheria, scarlet fever, tuberculosis, and Malta fever and who helped to distinguish between louse-borne and murine typhus. His chief distinction lies in his being credited with the discovery that typhus fever is transmitted by the body louse. His contributions to medicine were given recognition by Tunisia on a postage stamp issued in 1952 and by France in 1958.

Armauer Hansen (1841-1912) was a Norwegian physician who discovered the leprosy bacillus. A postage stamp in his honor and in celebration of the International Leprosy Congress at Havana (1948) was issued by Cuba in 1948. Also Brazil in 1948 and Belgium in 1964 commemorated Hansen's contribution to medicine.

*See Minnesota Med 50:201, 1967.

**See Test Your Word Score Page 363.

Insulin Preparations

Their Actions

WILLIAM R. KIRTLEY, M.D.*
Indianapolis, Indiana

A DECADE has passed since the advent of oral therapy for the treatment of diabetes mellitus. The first such preparation, a sulfonylurea, was designated Carbutamide, or BZ-55, the numerical portion of the title indicating the approximate year of beginning interest.¹

In ten or more years a new therapeutic approach for an important disease can be fairly completely explored, to the point where the subject has little appeal to the medical writer, or, for that matter, to the medical reader. While there still remain a number of extremely important scientific truths to be spelled out regarding the mode of action of the sulfonylureas, the clinical application of these agents has become much a matter of routine and these drugs are, in the minds of many, the first therapeutic tools to be used once the diagnosis of maturity-onset, nonketotic diabetes has been made. It can even be said that on occasion the sulfonylureas may be employed in place of diet therapy, rather than ancillary to this more basic consideration.

Diabetic patients have remained the same. It is only that we now catalogue them differently and a different attitude prevails. Where previously the feeling was that in case of doubt use insulin, the current, perhaps unvoiced, opinion is expressed as: when all else fails, use insulin!

Assuming, however, that the decision has been reached that insulin is to be employed, what logical sequence can be followed to establish the best possible control for the particular patient?

Without becoming embroiled in a precise definition of what constitutes the best possible control, let us agree that the closest approach to continuous normoglycemia, without the production of inadvertent hypoglycemic episodes, will be the goal that is sought.

*Lilly Research Laboratories.

Diet Is Still Essential

In any attempt at diabetic control, the preliminary steps have remained unaltered. Insulin requirements can be determined with a fair degree of accuracy only when dietary regulation has been simultaneously, or in some cases previously, established. Quite commonly the diabetic is overweight, but even if he is not it is easier to bring about good management if, initially at least, a restriction is placed on total caloric intake.² Once an insulin response is obtained, it is fairly easy to increase the diet in a stepwise fashion until intake equals requirement, related to sex, age, body build, and occupation.

Choice of Insulin for Initial Therapy

Depending upon the severity of the diabetes encountered and the rapidity with which control needs to be established, a choice will be made between soluble, rapidly acting regular insulin and one of the modifications. At this initial point it is impossible to judge the type of response that may be obtained, and in the absence of acidosis (*mild* ketosis not presenting quite the

same degree of urgency) it is acceptable to use a longer-acting insulin.

Intermediately-Timed Insulins

Experience has shown that either Lente insulin³ or NPH insulin,⁴ so-called intermediately timed insulins, will be effective in some 80 to 85 percent of insulin-requiring diabetics. Therefore, it is reasonable to start with one of these modifications and to adjust dosage depending upon response. Such diabetics can be adequately controlled as outpatients⁵ once they are taught a method of urine testing and of course given diet instruction. Also, it is essential that they understand insulin administration, so that they may follow telephone instructions on dosage adjustment, if required.

It is of great help to the physician to have available a blood-sugar value fasting which can serve as a rough guide for the first dose of insulin. If the blood sugar is under 200 mg. percent, 10 units would be an acceptable initial dose; if over 200 mg. percent, then probably 20 units would be more suitable.

Urine-sugar values should be recorded by the patient four or five times daily, and daily adjustment in insulin can be ordered. If urine tests are persistently 3 or 4+, the basic dose can be increased four or five units each day until the glycosuria clears, or at least does not exceed 2+.

A precautionary note may be helpful. As urine sugars begin clearing it is frequently necessary to question patients closely regarding the occurrence of symptoms of hypoglycemia, since they may assume that hunger and nervousness are natural correlaries of restricted food intake. Actually, a judicious cutback in insulin dosage may be indicated before really serious hypoglycemia becomes manifest.

Usually, six to ten days will be required to establish the routine insulin dosage. Once this is accomplished, a stepwise increase in food intake can be initiated, if desirable. From a base line of 1200 calories per day, increments of 300 to 400 calories can be added, and not uncommonly these increases are possible without a need for insulin adjustment, a certain degree of tolerance to

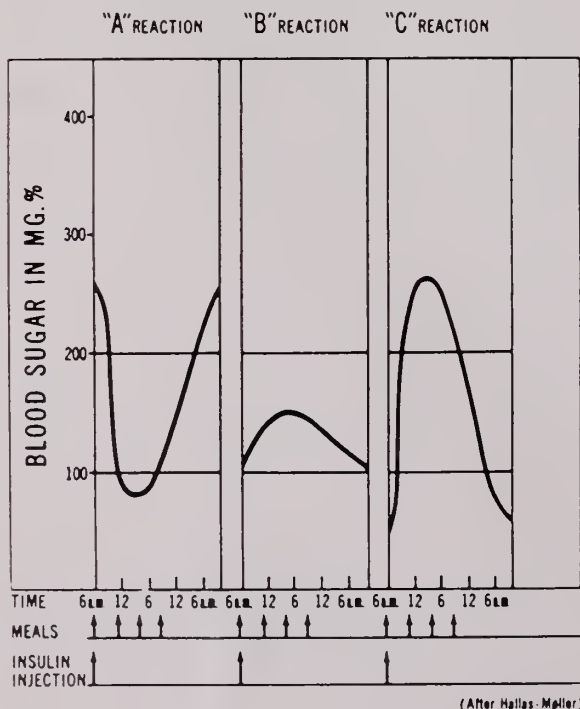


Fig. 1 — Types of response to a single daily dose of NPH insulin.

carbohydrate being regained during the normalization of the blood sugar by the use of insulin. A final maintenance dietary level of 1800 to 2500 calories should be the goal.

Regular Insulin as the First Choice

A patient may exhibit symptoms requiring a somewhat more rigorous approach to control, and especially so if ketosis is apt to progress into acidosis. In these circumstances regular insulin needs to be considered of first importance, since it is imperative to reverse the ketotic process as rapidly as is compatible with safety.

Using the previously described method of fractional urine testing, regular insulin is given on a scale of 4 or 5 units for each plus value, before meals and again at bedtime, if necessary. Obviously it is desirable to transfer the patient to modified insulin as soon as possible. This can be initiated on the second day of therapy by taking approximately one half to three fourths of the total insulin dose of regular insulin and converting to Lente or NPH insulin. This amount is given in the morning before breakfast, and again supplements of regular insulin are given on the following day. Subsequent increases in the basic dose of modified insulin will depend upon the amount of supplemental regular insulin required.

For these relatively stable diabetics, the routine is fairly easy to establish. Since perhaps 80 percent of the insulin-dependent group fall in this category, these measures should be given first consideration. The real problems lie in the remaining 20 percent. These patients have the typical juvenile, labile diabetes and frequently require customizing of the insulin regime. Here one can use to good advantage the other modifications of insulin, such as Semi- and Ultralente, and various mixtures or multiple-dose technics.

There can be no set rules. Only general principles can be outlined, and an understanding of the scope and limitations of each type of insulin must be in hand.

Actions of Insulin Modifications

Insulin preparations are classified according to their time activity, which is a con-

venient method for comparing one modification with another. However, it must be realized that this specific action cannot hold for all diabetics and that patient variations in response to any single preparation will be encountered.

Normal Reaction

In the average patient, regular insulin reaches a peak of activity in thirty minutes to one hour and has a duration of five to seven hours. Individual patients, however, may react in patterns that are entirely different. An extreme example, and admittedly a rather rare one, is the patient who gets along quite well on a single dose of regular insulin given in the morning before breakfast, requires no further supplemental insulin, and yet without this single dose exhibits hyperglycemia and glycosuria throughout the day.

Variation in patient response is probably more commonly encountered when the modified insulins are used. As an example, Lente and NPH insulins have similar effects. On an average, onset occurs in an hour or two and peaks in four or more hours, with a duration of approximately 28 to 30 hours; yet, as is frequently seen, responses on both sides of this norm are encountered.⁶

Short Reaction

In some patients the action is far too short in duration and concurrently the onset is too rapid. This response will be reflected in the clinical findings of low blood-sugar values during the late morning and early afternoon, with a rising sugar in the evening, or at least over the sleeping hours, accompanied by nocturnal glycosuria (Figure 1-a).

Prolonged Reaction

Quite the reverse situation can also be seen. In some there will be a lag in onset, with a prolongation of hypoglycemic effect, so that mid-day hyperglycemia will occur in the face of low or normal fasting sugar levels (Figure 1-c).

These responses have been graphically represented by Hallas-Møller⁷ and described

as the "A" curve, "B" curve, and "C" curve, in which the "B" curve is the normal desirable response (Figure 1-b).

Correction of Distorted Blood Sugar Curves

It can be readily seen that if one attempts to control either situation by merely increasing the dose of Lente or NPH, the distorted curve will be reinforced and the threat of deeper hypoglycemia will become manifest. Only a change of emphasis will remedy the situation. In the first instance, it would seem that an insulin with longer action would be helpful, as indeed it is in some cases. This would be the type of patient response in which Ultralente in combination with the basic Lente dosage, or more rarely alone, would have a desirable effect. Since Ultralente and Lente are chemically identical, mixtures can be prepared at will without any concern for the ratio of the mixture.

Twice Daily Administration

It should be kept in mind, however, that not all patients will achieve good control with one daily dose of any insulin or combination of insulins, and in these individuals two doses of the intermediate (Lente) insulin may be required.⁵ Usually, two doses, the first consisting of 60 to 80 percent of the total daily dose requirement, given before breakfast, and the remainder before the evening meal, will resolve much of the difficulty.

Should NPH insulin be used, one cannot as easily prolong its action, since Protamine zinc insulin or Ultralente should not be mixed with the NPH. Therefore, the split-dose technic is the approach that is recommended.

Mixture of Insulins

When a more rapid effect is desired, Lente insulin is subject to two approaches. Mixtures of Semilente insulin (whose activity is only slightly more prolonged than that of regular insulin) and Lente can be made in any desired ratio, since again the two preparations have identical chemical properties. Mixtures of regular insulin and Lente insulin do carry some restrictions, but only

insofar as the ratio of the two is concerned. It has been determined that extemporaneous mixtures in which the ratio of regular to Lente is 1:1 or less are chemically compatible. Higher ratios can theoretically be less stable, since the pH of such a mixture will be lowered to a point where the insulin-zinc complex of the Lente becomes unstable and the prolonged action is lost.

Shortening the action of NPH insulin can be easily accomplished by the addition of regular. The NPH crystal is relatively stable; therefore, mixtures can be made with no concern for ratios.

The choice of insulin for the specific diabetic patient is a matter of fitting the action of the particular insulin or insulins to the type of diabetes encountered. Fortunately, most diabetics will respond to a satisfactory degree and in a sense "any insulin is good insulin," as was voiced by Dr. E. P. Joslin many years ago. Because of differences in response, there can be a place for Protamine Zinc insulin and Globin insulin, but as an indication of the over-all accepted use in the United States 55 percent of the total units of insulin used is in the form of NPH insulin, 20 percent as Lente insulin, 15 percent as Protamine Zinc insulin, and the remainder as regular, Globin, and the less generally applicable modifications, Semilente and Ultralente. Since Lente insulin and NPH have identical "timing," it is evident that the intermediate action is by far the most useful.

Insulin Allergy

On occasion, special situations will arise requiring the selection of insulin on a basis not necessarily related to timing of insulin release. Local sensitivity characterized by the appearance of redness, itching, and induration at the site of injection can occur early in the initiation of therapy. Fortunately, most such occurrences are self-limited and after a week or so the local reaction disappears and gives no further trouble. Antihistamines can be given orally with good effect in many cases, and on occasion mixing an injectable antihistamine with the insulin just prior to administration has been reported to be beneficial.

Experience has shown that in some cases the selection of insulin based upon the animal source and the use of pure beef or pure pork insulin can terminate local reactions, with more satisfactory response usually resulting from the use of beef-source insulin.

Single-species insulins are available. All modifications can be had made from beef pancreas and all except Semi- and Ultra-lente made from pork pancreas.

Insulin Resistance

A second type of response which can at times be improved by using single-species insulin is insulin resistance.^{8,9} Here the situation is reversed. Pork insulin has been shown to be more effective, presumably due to the fact that it more closely resembles human insulin in its amino-acid structure. Insulin binding or inactivation can be caused by specific antibodies, and such binding is seemingly less frequent with pork-source insulin in individual patients. Therefore, it is worth considering the use of pork insulin when high insulin dosage is encountered not due to dietary indiscretions.

Experimental Insulins in Resistance

Desalinated Pork Insulin

To effect an even closer resemblance of pork insulin to human insulin, it has been possible to remove a single variant in the amino-acid sequence of pork insulin, so that the remainder is identical to human insulin. Alanine is the variant and, being the terminal amino acid in the "B" chain of insulin, can be removed by enzymatic action without significantly altering the biological activity of the insulin. The use of this altered insulin can, in some cases, result in an added increment of dosage reduction. This specially treated insulin has been designated desalinated pork insulin, which for convenience has been shortened to Dalanated pork insulin.^{8,9} It is as yet only experimentally available.

Sulfated Insulin

A second preparation in the same state of

experimental use is so-called Sulfated insulin.¹⁰ In this instance insulin is treated with sulfuric acid in such a way that a certain amount of denaturation occurs and presumably is no longer recognized as an antigen by the insulin-binding antibodies. Although the experience is small, marked reduction in insulin dosage has been reported in some severely resistant patients. Sulfated insulin is not available in the United States and currently can be obtained only in Canada.

Other New Developments

Two new modifications of insulin have been available on a limited basis, but as yet proof of definite improvement in the control of diabetes is not available. These preparations, known as Actrapid and Rapitard insulin,¹¹ differ from the Lente modifications only in the fact that the total zinc content is reduced to approximately one tenth.

Much of a sensational nature has appeared in the literature concerning synthetic insulin, particularly in reference to the recent report coming from China indicating that total synthesis has been effected.¹² This is indeed a fact but should be regarded as only one step in a long series of experiments which have been conducted in a number of research centers, both in the United States^{13,14} and in Europe,¹⁵ as well as in China. The likelihood of the availability of clinical supplies of synthetic insulin in the near future is quite remote. These reports of progress of synthesis are important in their own right and may be quite helpful to scientists in devising tools to assist in a better understanding of the action of insulin and other metabolic processes.

Summary

Insulin therapy still remains the keystone in definitive therapy of diabetes mellitus. The severe, acute complications of the disease, ketosis, acidosis, and coma, can be treated only with insulin. The use of insulin in the routine management of diabetes continues to increase year by year, and the principles of management have remained unchanged. A review of the practical considerations of such management is presented.

References may be secured from the author or the reprints.

Aphorisms of Maimonides (1135-1204)

Part I

1. Man is bound to lead a life pleasing to God if he wants to have a healthy body, and he must hold himself far from everything that can hurt his health and accustom himself to whatever renews his strength.

2. A man must not overload his stomach but be content always with something less than is necessary to make him feel quite satisfied. He should not drink much during the meal and only of water and wine mixed, taking somewhat more after digestion has begun and after digestion is completed, in moderation according to his needs.

3. Food should be taken always in the sitting position. There should be no riding nor walking, nor movements of the body until digestion is finished. The man who takes a walk or any strenuous occupation immediately after eating subjects himself to serious dangers of disease.

4. Day and night should be divided into twenty-four hours. Men should sleep for eight hours, and so arrange their sleep that the end of it comes with the dawn, so that from the beginning of sleep until sunrise there should be an eight-hour interval.

5. During sleep a man should lie neither on his face nor on his back but on his side, the beginning of the night on his left and at the end on his right. He should not go to sleep for three or four hours after eating and should not sleep during the day.

6. Fruits that are laxative, as grapes, figs, melons, gourds, should be taken only before meal time and not mixed with other food.

7. Eat what is easily digestible before what is difficult of digestion. The flesh of birds before beef and the flesh of calves before that of cows and steers.

8. In summer eat cooling food, acids, and no spices. In winter, on the contrary, eat warming foods, rich in spices, mustard, and other heating substances. In cold and warm climates one should eat according to the climatic conditions.

9. There are certain harmful foods that should be avoided. Large salt fish, old cheese, old pickled meat, young new wine, evil-smelling and bitter foods are often poisonous. There are also some which are less harmful, but are not to be recommended as ordinary nutritive materials. Large fish, cheese, milk more than twenty-four hours after milking, the flesh of old oxen, beans, peas, unleavened bread, sauerkraut, onions, radishes and the like. These are to be taken only in small quantities and only in the winter time and they should be avoided in the summer. Beans and lentils are to be recommended neither in winter nor summer.

10. As a rule one should avoid the eating of tree fruits, or not eat much of them, especially when they are dry and even less when they are green.

11. The fruits that are to be recommended dry as well as fresh, are figs, grapes and almonds.

12. Honey and wine are not good for children, though they are beneficial for older people, especially in winter. In summer one-third less of them should be eaten than in winter.

The Regulation of Insulin Secretion

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INSULIN IS IN many ways the best known of all hormones, and yet mystery and controversy continue to be associated with many aspects of its role in the economy of the human being. There is no disagreement, however, concerning the importance of insulin in body metabolism. Regulation of insulin secretion from the pancreatic islet seemed not long ago to be a relatively straight-forward and well-understood matter; now, however, in the light of recent information, it appears likely that it is a far more complex problem than had been realized.

There is at present considerable disagreement concerning the role of insulin deficiency or of inadequate insulin secretion in the common form of diabetes (the stable "adult" variety) and in the beginning stages of juvenile diabetes. Even if some degree of insulin deficiency proves not to be the first event in the development of human diabetes, it seems highly likely that disordered insulin secretion plays a major role in the established metabolic disturbance.

It is curious that sulfonylurea drugs, such as tolbutamide, now widely used in the treatment of diabetes, are capable of increasing secretion of insulin from the pancreatic beta cells even though the elevated blood glucose concentration in these subjects is no longer able to provoke a normal response. While it may be that increased insulin secretion is not the entire explanation for the hypoglycemic effect of these drugs, their action on the beta cell clearly points to the possibility that blood glucose concentration may not be the sole determinant of insulin secretion.

It is the purpose of this brief review to point out the fascinating variety of recent information which indicates that other factors than blood glucose may play an important part in insulin regulation. Attention will be restricted primarily to physiological

substances. For a detailed bibliography, the interested reader is directed to references given below.^{1,2}

Glucose and Insulin Secretion

Direct Effects of Glucose

When insulin was identified as a hormone, it was natural to assume that its secretion would be regulated in some manner by glucose, the substance most obviously associated with the action of insulin in the body. Indirect evidence that insulin secretion could be provoked by glucose was furnished by animal experiments in which local injection of glucose into the arteries supplying the pancreas — especially a transplanted pancreas — led promptly to a *drop* in blood glucose in the general circulation of the experimental animal.

However, it was not until the recent advent of sensitive and specific assays for insulin itself in blood that direct confirmation of insulin release following glucose administration was obtained. By now an overwhelming number of studies have made it clear that in human beings and in many other animals administration of glucose by several different routes leads to a prompt and striking increase in insulin concentra-

tion in pancreatic venous as well as systemic blood.³

It is also very natural to infer from such experiments that it is the glucose molecule itself, reaching the pancreatic beta cell, which in some manner excites secretion of insulin directly at its source. Strictly speaking, however, such evidence is not furnished by experiments in intact human subjects or intact animals, in which glucose clearly reaches all other tissues in the body as well as the beta cells. Ideally, the beta cell should be studied apart from any other cell or tissue; to my knowledge no such study has as yet been successfully performed. The closest approaches so far have been to isolate the rat pancreas and to perfuse it *in vitro* (albeit with a portion of gut and spleen attached) (Grodsky and others) or to study slices of the whole rabbit pancreas *in vitro*.⁴ Such studies do indeed show a prompt outpouring of insulin on exposing the preparation to increased glucose concentration. Grodsky has shown that the response is very swift, occurring in about 30 seconds after the increase in glucose, and also shutting itself off just as quickly when glucose concentration has fallen back to baseline levels.

It is worth noting that it has not been

LIVER- β CELL CYCLE (PROPOSED)

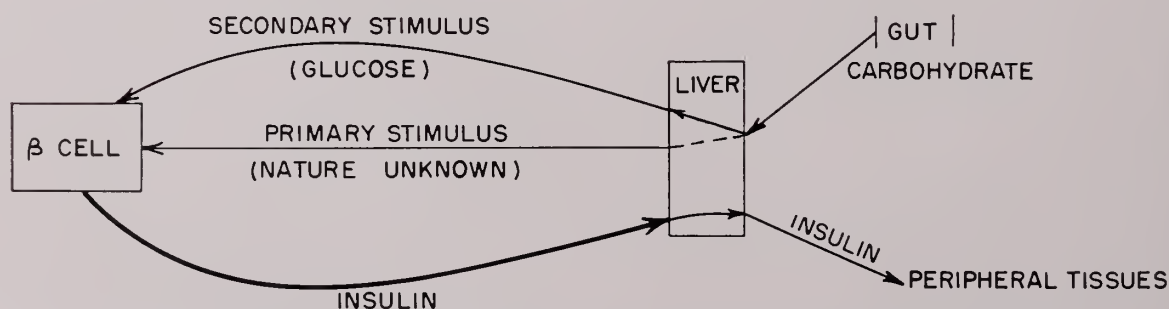


Fig. 1 — A diagram illustrating the idea that metabolism of carbohydrate in the liver may set off an early signal to the beta cell to release insulin, before any rise in the concentration of glucose bathing the beta cell has occurred. The location of such a carbohydrate-responsive receptor in the liver is hypothetical.

possible to determine the minimum sensitivity of the beta cell to glucose — the smallest rise in blood glucose which will set off increased insulin secretion. Such information, if secured in an isolated pancreas preparation, might not be relevant to what goes on in the intact human or animal. Furthermore, the possibility that there may be interaction between the different kinds of cells in the pancreatic islet, or between the cells of the digestive portion of the pancreas and those of the islet, has in no sense been ruled out by the available studies. The following discussion will indicate that such interaction is no longer merely an academic possibility.

Insulin Secretion after Glucose, Not Mediated by Blood Glucose Level

While there appears no reason to doubt the direct effect of blood glucose on the pancreatic islet — and probably the beta cell — at least two kinds of evidence have appeared in recent years to suggest that the action of glucose may not be solely restricted to such a direct effect. Several studies have compared the effect on blood insulin levels of glucose given by mouth vs. glucose given into a peripheral vein; the experiments of Elrick and others⁵ are typical. Blood insulin levels were strikingly higher in normal human subjects following glucose given by mouth, in comparison with levels after identical doses of glucose given by vein; blood sugar levels were if anything lower after the oral glucose despite the higher insulin response. This finding has lead to renewed interest in the possibility expressed many years ago that some substance or factor located in the gut itself might act as an insulin-releasing substance. In our own laboratory, using a wholly different approach, we have found that injection of small quantities of glucose into the portal vein — well beyond the pancreas, of course, — lead promptly to insulin release from the pancreas, even though no increase in blood glucose concentration is observed. This led to the suggestion that arrival of glucose in some tissue other than the pancreas — and perhaps in the liver itself — could set off some sort of a rapid signal

to the beta cells to begin insulin secretion, even before blood glucose had risen (see Figure 1).

These suggestions are not necessarily mutually exclusive. They have lead to some further interesting developments which will be described below.

Substances Other Than Glucose Which Lead to Insulin Release

Other Carbohydrates

The natural six carbon sugar *mannose* shares with glucose the ability to stimulate directly increased insulin output from the beta cell. This effect has been shown in the isolated animal pancreas, but mannose is also capable of inducing insulin secretion in the human being. Whatever the direct effect of glucose on the beta cell may be, the response to mannose suggests that it may not be a completely specific one.

It appears from studies of intraportal in-

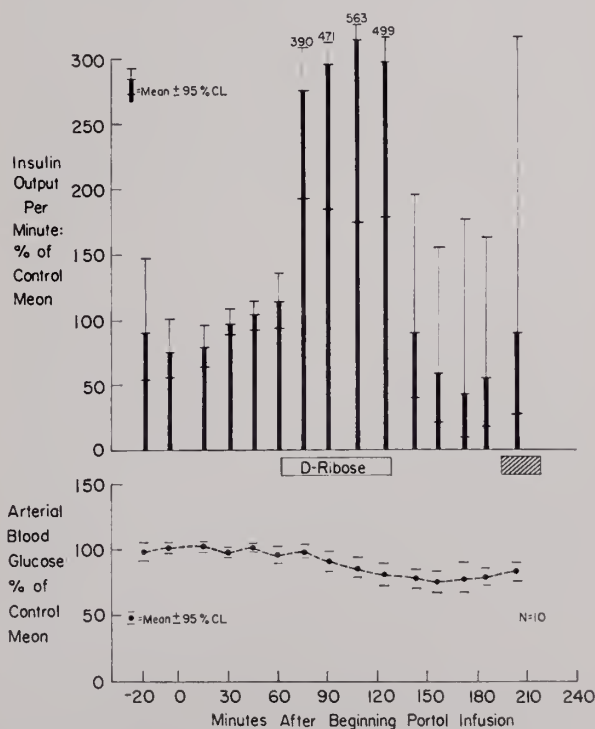


Fig. 2 — Summary of 10 experiments in normal anesthetized dogs showing the marked increase in pancreatic vein insulin output during intraportal infusion of ribose. Note that blood glucose concentration is slowly falling at the same time.*

*From Goetz, Maney and Greenberg: J Lab Clin Med, in press.

infusions of various sugars into dogs⁶ that two other natural sugars, galactose (six carbons) and ribose (five carbons) share the ability to evoke insulin secretion even though arterial glucose concentration is not raised or even if it falls. The effect of ribose is especially striking (see Figure 2). Subsequently we have observed prompt rises in peripheral blood insulin concentrations after giving ribose in normal unanesthetized dogs and in normal humans as well, despite the drop in blood glucose which has previously been known to follow ribose administration. Both ribose and galactose have been found to be ineffective in provoking insulin secretion in the isolated animal pancreas. Thus the possibility suggests itself that the metabolism of these sugars somewhere in the body — liver or elsewhere — leads to the rapid appearance of a "second messenger" of some kind which promptly increases pancreatic insulin output.

While neither of these two sugars is an important food constituent by itself, they can both be metabolized by normal mammalian tissues, share major metabolic pathways with glucose, and therefore suggest the possibility that they may share with glucose certain basic pathways for the regulation of insulin secretion.

Amino Acids

For many years a diet rich in protein has been considered to be the appropriate treatment for reactive or functional hypoglycemia in the adult subject. Recent findings on the effect of amino acids on insulin secretion are therefore something of a shock. Fajans and his collaborators have been especially active in investigating this area⁷. Their work stemmed from the observation that the amino-acid leucine promptly provokes hypoglycemia and insulin release not only in cases of the severe idiopathic hypoglycemia of infancy, but also in many adult subjects harboring an insulin-secreting islet cell tumor of the pancreas. It is now clear that leucine induces release of insulin and a modest drop in blood sugar even in normal subjects, but also that this effect is greatly exaggerated by pretreatment of the same

subjects with the sulfonylurea drug chlorpropamide (Diabinese[®]). Furthermore, a meal rich in protein produces elevations of plasma insulin levels considerably greater than those to be expected from the leucine content of the whole protein. Further study of a mixture of ten essential amino acids has shown that a number of these beside leucine are capable of inducing insulin release, and of these arginine is the most effective. The effectiveness of arginine, however, is not enhanced by prior treatment of the subject with chlorpropamide. Thus the mechanism of action may be somewhat different from that of leucine.

Fajans and his group suggest, from their *in-vivo* studies, that the amino acids themselves, and not their metabolites, may be directly affecting the pancreatic beta cells to cause insulin release. This matter is of course subject to further investigation in isolated pancreas preparations.

Ketone Bodies and Fatty Acids

Kipnis and others have shown that intravenous infusions of fatty acids into normal subjects are followed by elevation of blood insulin levels. This effect may not represent direct stimulation of the beta cell; however, according to the concept of the glucose-fatty acid cycle promulgated by Randle and others, elevated levels of nonesterified fatty acids in the blood may impair the ability of body tissues to respond to insulin, thus leading to a rising blood glucose concentration and a secondary stimulus to release of insulin. Also, beta-hydroxybutyric acid and acetoacetate have been reported to stimulate insulin release in anesthetized dogs. However, neither fatty acids themselves nor these products of fatty acid metabolism have been shown to stimulate insulin release directly *in vitro*.

Hormones, Including Glucagon

As has been noted above, several studies have indicated that glucose given by mouth is more effective than glucose by vein in provoking insulin release. This observation has led to an explosion of renewed interest in the possibility that the intestine may be

involved in the normal process of insulin release, by way of some mechanism triggered by the arrival of glucose in the intestinal lumen. There are at least three possible candidates for a hormonal intermediate in such a mechanism: glucagon, secretin, and pancreaticozymmin.

The possible role of glucagon may seem especially surprising at first glance, since it might be thought that the purpose of this substance in the body is to elevate the level of blood sugar by way of its well-known effect on increasing glycogen breakdown in the liver. However, it now appears that blood glucagon levels rise after the oral administration of glucose (but not after the intravenous administration); it also has been shown unequivocally that pancreatic glucagon is capable of exciting prompt insulin release from the isolated pancreas, where there is no simultaneous change in perfusing glucose concentration. It is possible that the intestine itself may contain glucagon or glucagon-like polypeptide which could be involved in the insulin release mechanism.

Further, while secretin and pancreaticozymmin have heretofore been primarily considered to be concerned with regulation of digestive activity of the pancreas, it now appears (from work especially of Dupré and Unger) that both of them can excite insulin release promptly when given by way of the portal vein in dogs or humans. Insulin release after pancreaticozymmin (but not after secretin) is accompanied by prompt rises in blood glucagon and glucose concentrations.⁸

The fact that these three substances can be shown experimentally to produce insulin release does not of course prove their role in the normal physiological response to glucose. The case for glucagon, however, is especially strong since it will release insulin in the isolated pancreas. In fact, since even in the isolated pancreas alpha cells (normally considered to be the principal source of glucagon in the body) are always present in intimate contact with the beta cell, it is at least theoretically possible that glucagon released from neighboring alpha cells could be an intermediate even in the so-called

“direct” release of glucose in the isolated pancreas.

Inorganic Ions

It appears that a minimal concentration of calcium is essential for the responsiveness of the isolated pancreas preparation to glucose and other substances. Thus this ion and perhaps a number of other substances may be important at least by way of a permissive effect. Potassium ion, in concentrations generally considered to be pathological (8 meq./L), has been shown to stimulate insulin release in the isolated organ.

Inhibition of Insulin Release

It was observed first in *in-vitro* studies and in animals, and later confirmed in human beings, that epinephrine and also norepinephrine are capable of suppressing insulin output with great effectiveness. In the human being this effect is especially striking since blood glucose rises sharply during intravenous administration of either hormone, while insulin levels remain low. As soon as the infusion of the catecholamine is ended, however, there is a very sharp and prompt rise in insulin levels, presumably due to the persisting high blood sugar concentration.

Recent work, especially by Porte (reviewed by Williams and Ensink⁹) has elucidated this interesting response further by the use of appropriate blocking agents in human studies. It appears that the suppressing of insulin response by epinephrine can be attributed to its alpha-adrenergic properties. When alpha-adrenergic receptors are blocked, it can be shown that epinephrine actually *stimulates* insulin release, this effect being mediated by beta-adrenergic receptors.

Neural Factors in the Regulation of Insulin Secretion

At the present time the greatest interest is centered on the possibility that humoral substances may mediate insulin release. However, it has been long known that both sympathetic and parasympathetic nerve fibers supply the pancreas, and that the possibility of neural control exists. The possibility of an important role by the vagus has been

strengthened by the demonstration by Frohman and others¹⁰ that electrical stimulation of the distal ends of both the left and the right vagus nerves in dogs produces sharp increases in insulin concentration in the portal vein.

Clinical and Physiologic Implications

The effect of blood glucose concentration on the beta cell is firmly established and it seems reasonable to assume that it plays a major role in the normal regulation of insulin secretion. It is now necessary, however, to consider the possibility that many other modifying factors may also play a significant part in insulin regulation. In fact, even the effect of glucose itself might be mediated by glucagon from the alpha cells of the islet. Furthermore, glucose may also act through another pathway remote from the pancreas (the ribose-responsive pathway).

Discovery of a "final common pathway" within the beta cell for the regulation of insulin release would resolve and simplify the present profusion of findings. Such a pathway would be sensitive to stimulation by glucose, mannose, and glucagon, and to suppression by epinephrine. It would also need to be sensitive to some signal — probably a metabolite — reaching it following the arrival of glucose or other carbohydrate

(such as ribose) and perhaps of amino acids as well, at a tissue site remote from the pancreas.

The nature of such a pathway must be a matter of pure speculation at the present. However, its sensitivity to both glucagon and epinephrine inevitably brings to mind the role of the cyclic nucleotide 3' 5' adenosine monophosphate (AMP) in the enzyme system for breakdown of glycogen.¹¹ To be sure, epinephrine and glucagon have very similar effects on liver glycogen breakdown, while their effects on the beta cell at present appear to be exactly opposite. In any case direct examination of this hypothesis will require direct study of the beta cell itself. See Figure 3 for a compilation of these ideas.

The most obvious and immediate *clinical* application of the material presented here relates to the management of the benign reactive or "functional" hypoglycemia seen in the adult, usually considered to be due to excessive insulin secretion after high carbohydrate intake. Since generous protein intake clearly can also lead to insulin release, the benefit of a very high protein diet in such persons now seems doubtful. The most sensible program would seem to be a regimen of frequent small meals containing

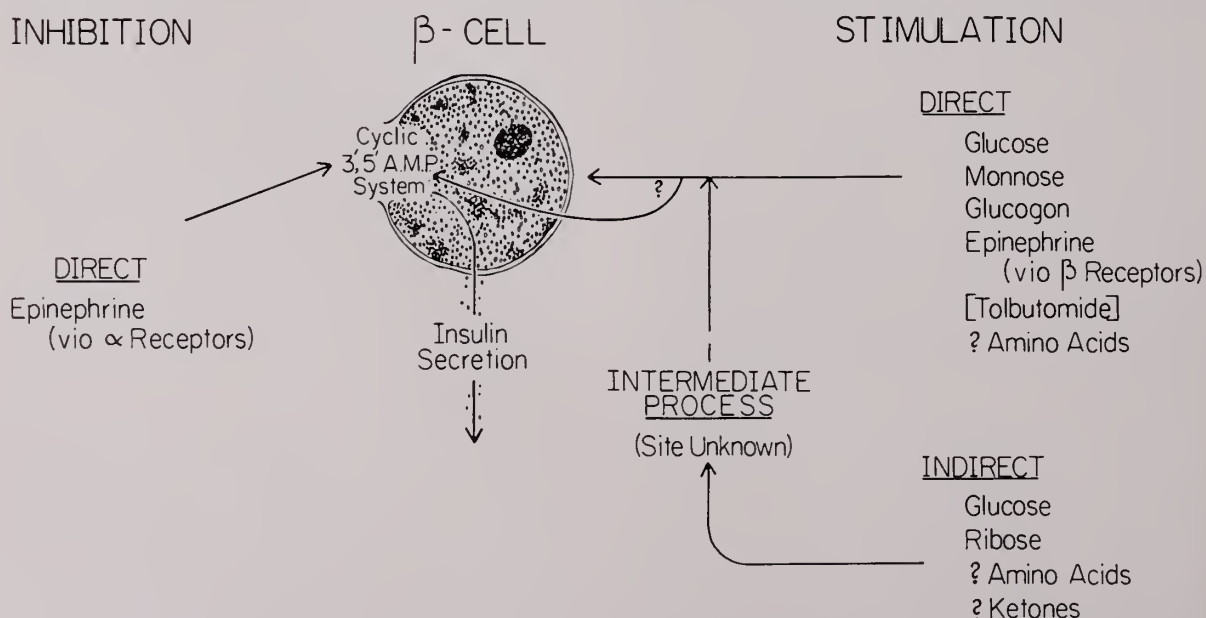


Fig. 3 — A diagram summarizing the factors which may play a part in the regulation of insulin secretion. Inclusion of cyclic AMP is hypothetical.

moderate amounts of both carbohydrate and protein.

While the newer information on insulin secretion has no immediate application to the clinical management of *diabetes*, there are important implications for the future. It seems likely that different forms or types of diabetes will emerge from the syndrome which is now characterized simply by hyperglycemia. In addition to the state characterized by a permanent incapacity of the beta cells to synthesize insulin (which is presumably the case in juvenile diabetes), it is likely that a syndrome may be defined in which the

capacity of the beta cells to synthesize and store insulin is perfectly normal, but the mechanisms for releasing this insulin are deranged. This may, indeed, prove to be the commonest form of diabetes — and also one in which rational treatment and even prevention may eventually be worked out.

Acknowledgment

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Dr. Stefan Fajans kindly furnished his typescript for review before publication.

References

1. Foà, P. T.: The Control of the Secretory Activity of the Islets of Langerhans. *Ciba Foundation Colloquia on Endocrinology* 9:55, 1956.
2. Grodsky, G. M., and Forsham, P. H.: Insulin and the Pancreas. *Ann Rev Physiol* 28:347, 1966.
3. Goetz, F. C.: Concerning the Validity of Different Methods for the Assay of Insulin in Blood. In *On the Nature and Treatment of Diabetes; Proceedings of the 5th Congress of the International Diabetes Federation, Amsterdam, Excerpta Med Foundation*, p. 181, 1965.
4. Coore, H. G., and Randle, P. J.: Regulation of Insulin Secretion Studied with Pieces of Rabbit Pancreas Incubated *in vitro*. *Biochem J* 93:66, 1964.
5. Elrick, H., Stimmler, L., Hlad, C. J., Jr., and Arai, Y.: Plasma Insulin Response to Oral and Intravenous Glucose Administration. *J Clin Endocr* 24:1076, 1964.
6. Goetz, F. C., Maney, J. W., and Greenberg, B. Z.: The Regulation of Insulin Secretion: Effects of the Infusion of Glucose, Ribose and Other Sugars into the Portal Veins of Dogs. *J Lab Clin Med*, in press.
7. Fajans, S. S., Floyd, J. C., Jr., Knopf, R. F., and Conn, J. W.: Effect of Amino Acids and Proteins on Insulin Secretion in Man. *Recent Progr Hormone Res* 22: in press, 1967.
8. (a) Leading article, *Intestinal Hormones and Insulin*. *Lancet* 2:35, 1966.
(b) Ketterer, H., Dupré, J., Eisentraut, A. M., and Unger, R. H.: Insulin-releasing Factors of the Gastrointestinal Tract (abstract). *Diabetes* 15:522, 1966.
9. Williams, R. H., and Ensink, J. W.: Secretion, Fates, and Actions of Insulin and Related Products. *Diabetes* 15:623, 1966.
10. Frohman, L. A., Ezdinli, E. Z., and Javid, R.: Effect of Vagal Stimulation on Insulin Secretion (abstract). *Diabetes* 15:522, 1966.
11. Sutherland, E. W., Øye, I., and Butcher, R. W.: The Action of Epinephrine and the Role of the Adenyl Cyclase System in Hormone Action. *Recent Progr Hormone Res* 21:623, 1965.

Abdominal Muscle Deficiency Syndrome

This syndrome consists of (1) partial or complete absence of abdominal musculature; (2) hydroureter, hydronephrosis, and megabladder; (3) undescended testes in males; and (4) malrotation of the intestine. Fröhlich described the first case in 1839. Fifty-eight cases have been reported to date (Mathieu *et al.*), only four of which were females.

Deficiency or absence of the abdominal muscles includes the lateral groups, the transversus, and the obliques. The recti are often present. Symptoms more often pertain to the genitourinary tract or to one of the other numerous congenital abnormalities. These include pigeon breast deformity, spina bifida with myelomeningocele, hydrocephalus, congenital bladder neck obstruction, bilateral hydroureter, urachus, and perhaps talipes. The clinical course is often complicated by episodes of infections that require antibiotics and possible surgery. Many of these patients have a low intelligence quotient and require chronic institutional care.

Durham, Robert H. — *Encyclopedia of Medical Syndromes*
Hoeber Medical Division, Harper and Row, New York

Magendie Before a Class of Medical Students

Here, gentlemen, is the heart of a young woman who recently died in this hospital. I believe that I have already published an account of her case, which is one of exceptional interest; but, however this may be, I remember perfectly well all the details of the results ascertained (during life) by a careful auscultation of her heart. The first sound was heard without any difficulty, but the second one was entirely lacking. What, it will be asked, was the cause of this phenomenon? At first I was disposed to believe that she was affected with hydrothorax, but, when I came to make a more careful examination, I was obliged to reject this hypothesis; and, although I suspected that the absence of the second sound was due to an obstacle of a mechanical nature, — one that nullified the stroke communicated by the heart to the sternum, — I was unable to form any idea as to the real nature of this obstacle. The present autopsy furnishes the desired explanation. As a result of a former attack of pericarditis the anterior surface of the heart was covered with a thick layer of false membranes; . . . the tip of the organ, on the other hand, still preserved its usual smooth and polished aspect. . . . In my judgment the interposition of false membranes, which had been deposited upon the surface of the heart, acted as a cushion, thus preventing the transmission of the sound by annulling the shock which would otherwise result from the blow upon the sternum. Lower down, at the tip of the organ, where no false membranes had been deposited, the blow upon the thorax, caused with each systole of the heart, produced the normal degree of noise.

— Francois Magendie (1783-1855)

A Case History

The man, whose case history I am about to relate, said that the symptoms from which he had suffered, during the preceding twelve months, were the following: a frequent but dry cough, with loss of appetite; almost constant thirst; difficulty in obtaining sleep; night-sweats, more marked in the region of the head and neck than elsewhere; and irregular chills and fever. The physicians whom he had consulted were led to believe that he was affected with consumption, and they treated him in accordance with this belief, but so far without success. On examination I found that two of his teeth were carious, and I advised their extraction. A rapid restoration of the patient's health followed in less than a fortnight.

— Jean Petit (1674-1760)

The Middle Ages may have been a time of salutary delay. If it had exploited the earth's surface as we are doing, we would perhaps not be around at all.

— Burckhardt

Love does not consist in gazing at each other but in looking together in the same direction. — Saint-Exupery

A painting teaches us to know a man; a photograph can but recall him to our minds. — Comtesse Diane

Management of the Pregnant Patient with Complicating Diabetes Mellitus

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Minneapolis, Minnesota

PRIOR TO the discovery of insulin in 1921 by Banting and Best the great majority of diabetic women were considered infertile. The cause of infertility was usually a secondary amenorrhea, presumably due to hypothalamic failure resulting from the constitutional disease. When diabetic women did occasionally become pregnant in the pre-insulin era some 25 percent of the mothers and about 50 percent of the infants died.¹ Most of the women died with the characteristic picture of acidosis and coma shortly after delivery. Now, with insulin and more careful diagnosis, many more pregnant diabetics are seen. An awareness of the problems of this association is essential.

Incidence

With good control of diabetes fertility is almost normal. Thus this disease is seen in 0.2 to 0.3 percent of all pregnancies. Two different types of diabetes mellitus will be encountered. Most of the cases are insulin-dependent-juvenile-type diabetes, but as diagnostic acumen has improved, more of the maturity-onset-type diabetes are being recognized. Many of these are first diagnosed during a pregnancy.

A large volume of data has accumulated in recent years which shows that normal pregnancy is a stimulus to the pancreas. As a result, beginning at the end of the first trimester and progressing to delivery, there is normally an increasing amount of circulating insulin. This pregnancy-induced pancreatic stress can be demonstrated both morphologically in pancreatic beta cell hyperplasia and biochemically as hyperinsulinemia.²⁻⁴ The mechanism of this pancreatic stress is unknown, but it may be a reaction to increased growth hormone (either of pituitary or placental origin), estrogen, cor-

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Presented at the South Dakota State Medical Association Meeting, Huron, South Dakota, May 23, 1966.

ticosteroids, or a placental insulin degradation ("insulinase") process.⁵ As a consequence of the unknown stress, late pregnancy becomes an ideal time to recognize those patients with limited pancreatic function. The characteristics of diabetes (or insulin deficiency as measured by blood glucose levels) may be found during pregnancy, only to disappear post partum. This has been termed "gestational" diabetes but is in reality early diabetes.

Diagnosis

The problem then is to alert the obstetrician to these changes during pregnancy and their interpretation. Tests for urinary sugars are frequently used. The urine of pregnant women often contains a reducing sugar which will give a positive Benedict's reaction. This could indicate: lactosuria, benign renal glycosuria, or diabetes mellitus. Since increased levels of blood lactose are normal near term and post partum, this reducing sugar should not be confused with the glucose of diabetes mellitus. During the last six weeks of pregnancy the frequency of lactosuria increases to about 8 percent and to 30 percent or more on the day before delivery. The more specific enzyme tests for glucose (glucose oxidase) will give a negative test with lactose.

Blood Glucose Abnormality

The increased renal blood flow and increased glomerular filtration rates associated with pregnancy will result in more molecules of glucose being brought to the renal tubules for any given blood glucose level. Benign renal glucosuria of pregnancy results. Because of this the diagnosis of diabetes mellitus during pregnancy can be made only on blood glucose abnormalities rather than on urine tests. Either a fasting blood sample or a glucose tolerance test can be used. Since there is an erratic gastrointestinal mobility and absorption during pregnancy it is advisable to use only the *intravenous* rather than the oral glucose tolerance test. This test eliminates the absorption variables and depends solely on utilization of the glucose load given. An example of the difference between the intravenous and oral test during pregnancy is

shown in Figure I. An erroneous diagnosis of diabetes mellitus would have been made from the oral test.

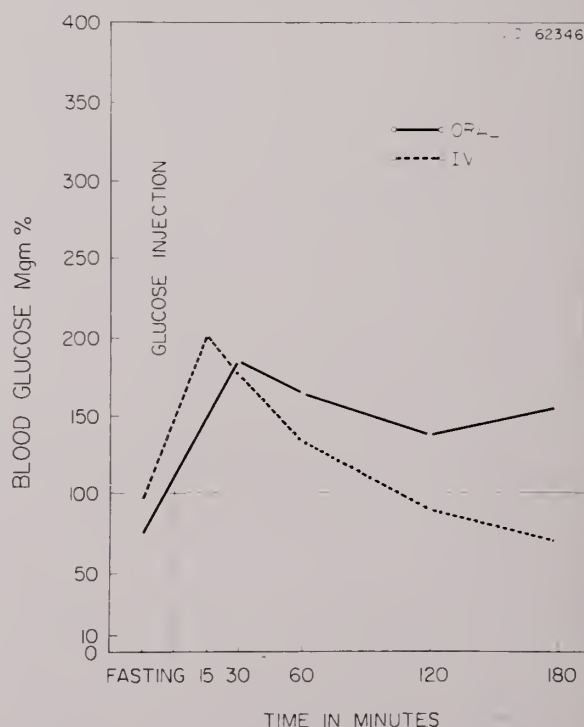
Management Dependent Upon Glucose Regulation

The glucosuria of pregnancy makes the clinical management of diabetics more dependent upon blood glucose regulation than on urine glucose control. Pregnant patients may have normal blood glucose levels and three to four plus urine glucose values. Treatment on the basis of urine glucose values in the usual way with a sliding scale for insulin dosage can result in maternal hypoglycemia.

Ketonuria

The glucosuria may be so severe in pregnant diabetics that most of their carbohydrate intake is lost into the urine. As a result their cellular metabolism will burn fat and produce mild ketonuria. This "starvation type" ketonuria is not serious and must be differentiated from true diabetic ketoacidosis where high-serum ketone-body levels are

GLUCOSE TOLERANCE TEST IN PREGNANT WOMAN



Blood glucose values for an oral and an intravenous glucose tolerance test on one-term pregnant patient performed at a three-day interval.

found. It can be treated by measuring the 24-hour urine output of glucose and increasing the carbohydrate content of the diet accordingly.

Maternal Problems

The maternal problems in diabetes during pregnancy include: shifting insulin requirements, hypoglycemia, acidosis, toxemia and hydramnios.

Shifting Insulin Requirement

With the known increased output of insulin by the pancreas in a normal pregnant patient it would be presumed that patients with pancreatic insulin deficiency, that is, those with juvenile diabetes mellitus, would need more exogenous insulin during pregnancy. Indeed, in most clinical series it has been shown that the majority of patients with diabetes will need more insulin during pregnancy.

Hypoglycemia

The extremes of glucose control present problems at different times during pregnancy. In the first half of pregnancy hypoglycemia is generally the problem. A common pattern is for the patient to take her morning insulin, eat breakfast and then because of "morning sickness," vomit her carbohydrate intake and become hypoglycemic.

Acidosis

Maternal acidosis becomes a problem primarily in the last half of pregnancy. There are several probable reasons for this: the increased need for exogenous insulin is not adequately satisfied²; there is a natural tendency toward acidosis in pregnancy, due to the diminished carbon dioxide combining power of the blood, and the frequent glucosuria in late pregnancy makes urine glucose values unreliable in the detection of impending ketoacidosis. The problem is very serious because almost all of the maternal deaths in diabetics today are due to acidosis, and there is a high association of fetal death in utero with maternal acidosis.

Toxemia and Hydramnios

The remaining two problems, toxemia and hydramnios, are associated with salt and wa-

ter retention. The incidence of toxemia in uncomplicated pregnancies is about 7 percent but in diabetics rises to 25 to 50 percent.⁶ The incidence of hydramnios in uncomplicated pregnancy is less than one percent, but in the pregnancies of diabetic women it is 5 to 30 percent.⁶ Both of these conditions are associated with a high frequency of fetal death in utero. There is no evidence that pregnancy per se will change the ultimate prognosis or course of diabetes mellitus.

Infant Problems

The babies of diabetic mothers present several problems which include fetal death in utero, congenital abnormalities, hypoglycemia, hyaline membrane disease, excessive size and diabetes mellitus.

Fetal Deaths

There is no increase in the abortion rate. The frequency of stillbirth is known to rise from mid-pregnancy until term and to be higher than in non-diabetic pregnancy. This is closely associated with acidosis and also with other maternal complications.

Congenital Abnormalities

The incidence of congenital abnormalities is about three times that seen in infants of normal mothers. Pedersen has shown the frequency to be directly related to the severity of the maternal diabetes.⁷

Excessive Size

The infants of diabetic mothers are usually larger than other infants, primarily due to fat deposition, and thus there is less body water per kilogram weight. There is also organomegaly. If severe maternal vascular disease is present small infants may result. Many factors may contribute to the large infants, including genetic factors, a hyperglucosemic environment (glucose readily passes the placental barrier), and increased production of growth hormone and insulin by the infant. The incidence of babies weighing 10 or more pounds, born to diabetic mothers, ranges in reported series from 15 to 25 percent, whereas this occurs in only 3 percent of non-diabetic mothers. Mothers

who have produced excessive-sized babies should be carefully investigated for diabetes. In experimentally produced alloxan* diabetes in rats, fetuses of excessive size were produced four times more frequently than in controls.⁸

Prognosis

Maternal

The risk for the diabetic mother is now very low. Hagbard found an over-all maternal mortality of 0.7 percent in 2,496 collected cases.⁹ Almost all maternal deaths today from diabetes complicating pregnancy are due to neglect.

Fetal

Most of the series reported an over-all perinatal mortality of about 15 percent. This varies, however, with the severity of the mother's disease. Since diabetes is associated with vascular disease and the severity of the vascular sclerosis is related to the duration of the disease, White et al. have devised a classification scheme of maternal disease severity from A through F. The perinatal mortality is directly related to the class of the mother's disease.¹⁰ Most authors agree that for a given class, the better the diabetic control (normal blood glucose values) the better the perinatal survival.

Management

In order to combat the complications listed above several principles of management are proposed.

Visits

It is suggested that the pregnant diabetic patient be managed by a team consisting of an obstetrician, an internist and a pediatrician. The patient must be seen frequently, at least every two weeks during the prenatal period. When any problems arise hospitalization should be arranged. Pedersen in Denmark has obtained excellent results by superb control during hospitalization for the last eight weeks of pregnancy.

Insulin

An important principle is to maintain nor-

mal blood glucose levels. This can be done by keeping the patient's diet and activities constant and adjusting her insulin dosage. The required insulin dose will increase in approximately two thirds of the patients; the remainder may need less or the same amount. The type of insulin used is not important. Since urine sugars become of little value during pregnancy, frequent fasting and postprandial blood glucose values must be obtained. Occasional quantitative checks of 24-hour urine glucose spillage is also helpful. A positive ketone body urine test should be checked with serum ketone levels. The insulin requirement usually decreases by one third to one half immediately post partum but by six months post partum is at the pre-pregnancy level. Insulin probably does not cross the placenta so that it will not harm the fetus. A falling insulin requirement near term is a poor prognostic sign, probably indicating decreased placental function and decreased "insulin-antagonist" production.

Diet

A constant dietary intake is essential for good control. White recommends 30-40 calories per kg. daily, including 150-250 grams of carbohydrate, 2 gm./kg. of protein, and the remaining calories in fat. In order to reduce water retention, a low sodium intake is begun at the first visit (2 grams Na.). The use of diuretics is also helpful, as they decrease the severity of toxemia and hydramnios but unfortunately not their incidence. The thiazide diuretics may raise blood glucose levels, but this can be controlled with more insulin if necessary. Breast feeding is not contraindicated, but a compensatory increase in dietary intake must be made. White has used exogenous estrogen and progesterone in treatment, but others have achieved as good results without these hormones.

Delivery

Because the incidence of fetal death in utero rises until term, it is recommended that infants be delivered between the 36th and 37th weeks of gestation, assuming that the infant is correspondingly mature. At this point one obtains the greatest total fetal

*See Test Your Word Score Page 363.

survival with an optimal relation between the risk of fetal death in utero and neonatal death from prematurity. Vaginal delivery following induction of labor is chosen when the usual criteria are favorable; but frequently at this period of gestation cesarean section becomes the only feasible means of delivery. The measurement of serial 24-hour urinary excretion of estriol has aided in the timing of deliveries, and a falling level is a poor prognostic sign, as shown by Greene.¹¹

Newborn Management

Since the infants have frequently been exposed to excessive amniotic fluid and have full stomachs at birth, immediate gastric suctioning is advised. They should be watched for hypoglycemia and respiratory distress and treated accordingly. Although the infants frequently have large birth weights, the organ systems do not always

function with corresponding maturity. Some authorities therefore recommend that during the first 72 hours of life these infants be treated with extra care. This includes an atmosphere of 40 to 50 percent oxygen, increased humidity, a temperature of 85°F. and frequent nursing observations.¹² Since diabetes has a hereditary tendency, there is an increased risk of diabetes in these infants in later life.

Summary

The management of pregnant patients with diabetes mellitus is becoming a more frequently encountered problem for physicians. A review of the problems involved and their treatment is given.

Acknowledgment

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References

1. Duncan, M.: On Puerperal Diabetes. Trans Obstet Soc London 24:256, 1882.
2. Spellacy, W. N., Goetz, F. C., Greenberg, B. Z., and Ells, J.: Plasma Insulin in Normal Early Pregnancy. Obstet Gynec 25:862, 1965.
3. Spellacy, W. N., Goetz, F. C., Greenberg, B. Z., and Ells, J.: Plasma Insulin in Normal Mid-Pregnancy. Amer J Obstet Gynec 92:11, 1965.
4. Spellacy, W. N., and Goetz, F. C.: Plasma Insulin in Normal Late Pregnancy. New Engl J Med 268:988, 1963.
5. Spellacy, W. N., Carlson, K. L., and Birk, S. A.: Dynamics of Human Placental Lactogen (HPL). Amer J Obstet Gynec In Press.
6. Kyle, G. C.: Diabetes and Pregnancy. Ann Intern Med Suppl 3:59:1, 1963.
7. Pedersen, L. M., Tygstrup, I. and Pedersen, J.: Congenital Malformations in Newborn Infants of Diabetic Women — Correlating with Maternal Diabetic Vascular Complications. Lancet 1:1124, 1964.
8. Lazarow, A., Kim, J. N., and Wells, L. J.: Birth Weight and Fetal Mortality in Pregnant Subdiabetic Rats. Diabetes 9:114, 1960.
9. Hagbard, L.: Pregnancy and Diabetes Mellitus, in American Lecture Series No. 449, ed. by Hamblen, E. C., Charles C. Thomas, Springfield, Illinois, 1961.
10. White, P., Gillespie, L., and Sexton, L. I.: Use of Female Sex Hormone Therapy in Pregnant Diabetics. Amer J Obstet Gynec 71:57, 1956.
11. Greene, J. W., Smith, K., Kyle, G. C., Touchstone, J. C., and Duhring, J. L.: The Use of Urinary Estriol Excretion in the Management of Pregnancies Complicated by Diabetes Mellitus. Amer J Obstet Gynec 91:684, 1965.
12. Gellis, S. S., Hsia, D. Y.: The Infant of the Diabetic Mother. Amer J Dis Child 97:1, 1959.

Green Medicinals

Herbs for the Digestive Organs

Ecclesiasticus said: The Lord hath created medicines out of the earth and a wise man will not abhor them. Recommended for the digestive organs is a tonic easily infused for hops:

Hop Bitters

Take two ounces of buchu leaves and half a pound of hops. Boil together in an iron vessel in five quarts of water. When lukewarm add a pint of alcohol. — C. F. Level: Green Medicine

In addition to the lowly hops other aids to good digestion include convolvulus, Good King Henry,* meadowsweet, peppermint, rhubarb, silverweed, and Venus' looking-glass.*

*See Test Your Word Score Page 363.

Moliere on Doctors III*

The perennial hypochondriac vis-a-vis the exploiting doctor provides the theme for Moliere's Malade Imaginaire (The Imaginary Invalid), wherein the medical profession appears as a vast, autonomous entity: a monolithic, impersonal agency operating to perpetuate and vindicate its own power structure rather than to cure its humble patients.

In this farce Argan is the "imaginary invalid," whose bedroom ostentatiously displays a complete bar of medicaments prescribed by his physician, Dr. Purgon, one preparation for every malady that Argan is sure he is afflicted with.

Hitherto meek and obedient to his doctor's orders, Argan suddenly revolts at the prospect of being on the receiving end of a huge all-purpose syringe, to be administered by Dr. Purgon's apothecary. Outraged by his patient's heresy, Dr. Purgon shouts:

*"Here is a nice state of affairs! Never, in all my professional life, have I been so insulted. It was a Special and Most Extraordinary Mixture — never before administered to any living thing. One of my inspirations. It came to me, in one of the long watches of the night, and I arose — and prepared it for you, with my own hands. Every separate ingredient was to have had its own effect, upon your every ailment. It was to have cleansed your whole system — at one squirt. One squirt. I sent in my apothecary at the appointed moment, and he returned to me — the syringe unemptied, my miracle of healing unperformed — balked of his errand of mercy. And that constitutes not only a mortal insult to me personally, but to the whole Medical Faculty. You have destroyed, at one stroke, a sacred obligation — the unquestioning obedience of a patient to his physician. That is rebellion. The revolt of Ignorance against Authority. And in Medicine, as in Society, such behaviour must bring chaos and disaster. It cannot be tolerated. It must be nipped in the bud. And here and now. At once. And without mercy. You've brought this on yourself. I've done with you. I wash my hands of you. And leave you to your fate. Which — I may tell you — I don't envy you. In a short while from now, probably in a matter of hours, you will fall into a state of A-Pepsia. From that to U-Pepsia. From U-Pepsia to Mee-Pepsia. Then Drypsi-Pepsia. And from that in a condition of Bray-co-philial-Pepsia. And when the dread poison of that spreads into your every organ — as it must — then you will die — and horribly."****

Following this tirade Dr. Purgon departs in high dudgeon, abandoning the quaking Argan to his ordained doom — which, incidentally never materializes.

The Imaginary Invalid was written in 1673 and, like Moliere's earlier farces satirizing the medical profession, captivated French theater audiences with its witty dialogue and uproarious stage business.

*See Minnesota Med 50:116, 1967.

**Moliere: The Imaginary Invalid: Translated from the French by Miles Malleson.

Derivatively Speaking

Surgeon — from Greek *cheir* (hand) plus *ergon* (work)

On Quaffing

Where there's a swill there's a sway. — Magazine Digest

Renal Vascular Disease Associated with Diabetes Mellitus*

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DESPITE MASSIVE strides in unraveling the riddle of intermediary metabolism in diabetes and the successful treatment of hyperglycemia, glycosuria, ketonuria and diabetic coma, the cardiovascular complications of diabetes have increased in number and significance. This increase in complications seems to be due to the increased longevity of the diabetic, which enables a subtle and probably low-grade pathologic chemical stimulus to gradually evoke the vascular changes over a period of many years. The kidney is a major recipient of the damage resulting from vascular disease.

Materials and Methods

Studies have been made of the kidneys removed from human diabetic patients at autopsy and percutaneous renal biopsies of living patients with diabetes. Tissues have been fixed in either formalin or osmium tetroxide† and prepared for light or electron microscopy respectively. For light microscopy, two micron paraffin sections were stained with hematoxylin and eosin or the periodic acid-Schiff technique. For electron microscopy, tissues were embedded in epon, ultra-thin sections cut on a Porter-Blum ultratome-2, stained with uranyl acetate, and examined in a RCA EMU-3G electron microscope.

Arterial Disease

It is generally accepted that the diabetic develops intimal arteriosclerosis at an earlier age, also that it progresses more rapidly and is more severe at any given age than arteriosclerosis in the nondiabetic. As far as we know, there is no definite difference in the distribution of arteriosclerosis in the diabetic. However, it seems to manifest itself most obviously in the increased incidence of

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†See Test Your Word Score Page 363.

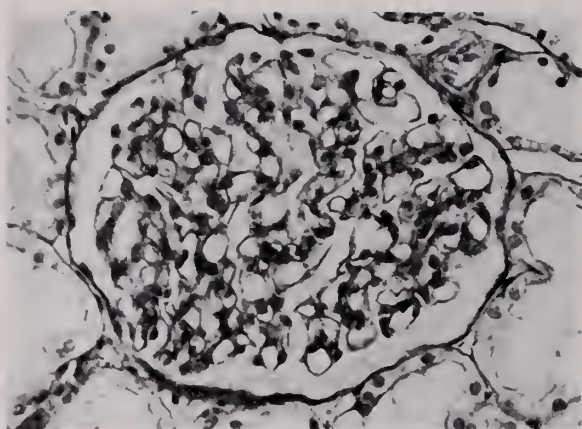


Fig. 1 — Normal human glomerulus showing the delicate stroma and regular capillary distribution. PAS-stain, 600 $\times$.

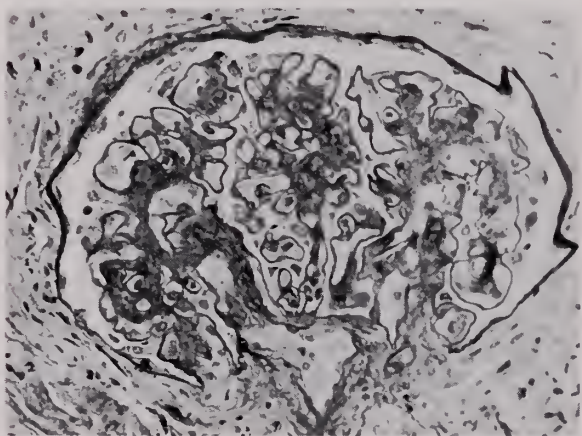


Fig. 2 — Glomerulus from diabetic patient showing diffuse glomerulosclerosis. Note the finely fibrillar thickening of the mesangial area throughout the glomerulus. PAS-Stain, 600 $\times$.

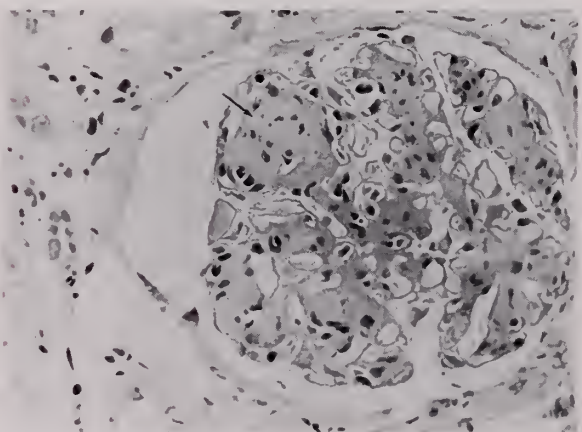


Fig. 3 — Glomerulus from a long-term diabetic patient showing typical nodular glomerulosclerosis (arrow), as well as diffuse glomerulosclerosis and transition stages. The nodules contain a few nuclei and have open peripheral capillaries. Hematoxylin and eosin, 560 $\times$.

coronary occlusions, especially in the female diabetic, and by a high incidence of peripheral gangrene.

Arteriosclerosis is exceptionally severe in the diabetic kidney. However, because of the large reserve of the kidney and the concurrent microvascular disease which seems to be more universally destructive, death of a diabetic due to arteriosclerosis of the kidney alone is rarely observed. On the other hand, arteriosclerosis plays a prominent part in the renal destruction which finally leads to uremia in many diabetics.

Most investigators have pointed out that there seems to be no morphological or chemical difference (except intensity) between the arteriosclerosis of the diabetic and the nondiabetic. Recently, several studies, including one from this laboratory, have indicated that there is a slight increase in the glycoprotein content of the arteriosclerotic aorta from a diabetic patient. By electron microscopy, this finding is explained by an increase in the basement membrane material of the artery of diabetics, just as basement membrane is increased in the capillaries. In the artery, basement membrane surrounds the external surface of the endothelial cells, just as it does in the capillaries, and also extends peripherally to separate and surround each smooth muscle fiber. All portions of this basement membrane network are thickened in the arteries of the diabetic. The significance of this thickened basement membrane in passage of nutrients and wastes is still under investigation, and conflicting opinions now exist.

Diabetic Microangiopathy

This term has been coined to include all the microvascular disease of the diabetic; namely, the retinopathy, the diffuse glomerulosclerosis, the nodular glomerulosclerosis described by Kimmelstiel and Wilson, and the diffuse basement membrane thickening of most peripheral capillaries. This author believes that this term should be reserved for microvascular disease which has an unquestioned relationship to basement membrane and its glycoprotein metabolism. At the present time, there is some question in

some quarters as to whether the microaneurysms and other focal changes of classical diabetic retinopathy are due to the diffuse basement membrane disease of retinal capillaries — although they may well be. The kidney lesions of diffuse and nodular diabetic glomerulosclerosis are unquestionably basement membrane-oriented and are properly classified as a subdivision of diabetic microangiopathy.

Diabetic Glomerulosclerosis

This term seems most acceptable for the sclerosing, often nodular disease of the glomerulus in diabetics. The term intercapillary glomerulosclerosis should be discarded since electron microscopy has shown that the lesions are not between the glomerular capillaries but within the basement membrane of the capillary tufts.

Diabetic glomerulosclerosis begins as an almost imperceptible increase in the normal mesangial stroma and a generalized thickening of all capillary basement membranes. Because of the wide variation in the normal and the technical problems inherent in measuring basement membrane thickness, it is difficult to be sure how early this basement membrane thickness begins (i.e., in the prediabetic), but after five to ten years of diabetes in most cases glomerular capillary basement membranes will show from one and one-half to two times the normal thickness. The normal mesangial stroma consists of a few very thin, widely dispersed bands or fingers of basement membrane-like material connected to the surrounding basement membrane and interdigitating between the cells of the mesangial area. The normal mesangial stroma has been called "basement membrane branches" and "mesangial matrix." We use the latter term for the normal mesangial stroma. When the bands or fingers of basement membrane-like material of the mesangial area become not only increased in number but also many times thickened by the diabetic process, we refer to it as "hyaline matrix" because of its resemblance to hyaline and to differentiate the pathologic state from the normal stroma.

Diffuse Form

The first stage of diabetic glomerulosclerosis is the diffuse form. In our experience and as reported by most observers, there is always thickening of the basement membrane at this time. Kimmelstiel seems to be the lone dissenter to this opinion. At the same time there is a mild increase in the mesangial stroma or hyalinoid matrix associated with proliferation of mesangial cells

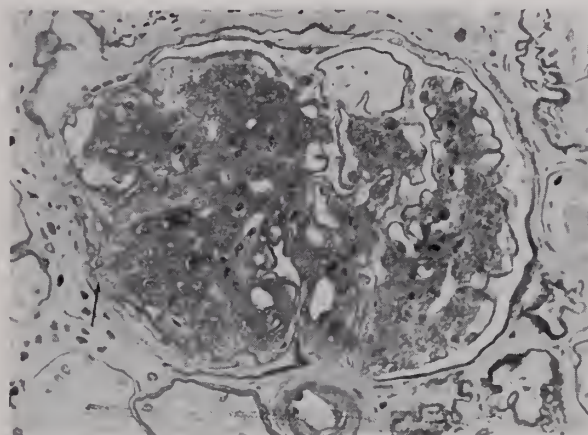


Fig. 4 — Glomerulus from a diabetic patient showing obliterative phase of glomerulosclerosis. Most capillary lumina have been occluded by the coalescence and expansion of nodules. Nuclei are beginning to disappear. One dilated capillary loop is present. Adhesions between the glomerulus and parietal Bowman's capsule are present (arrow). The arterioles show hyaline sclerosis. PAS-stain, 500 $\times$.

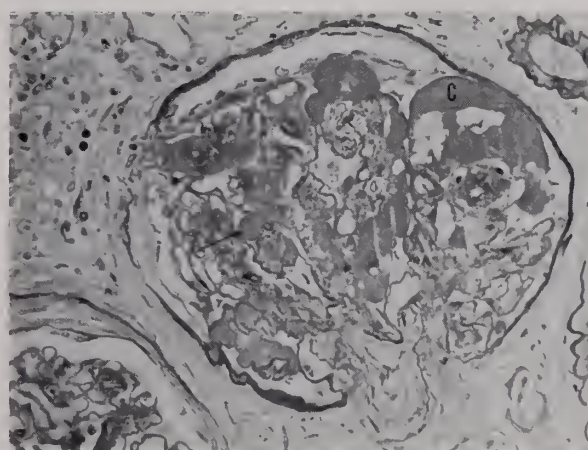


Fig. 5 — Glomerulus from a patient with long-term diabetes demonstrating exudative lesions. These lesions are dark and homogeneous in the photograph, with occasional areas of vacuolization. One crescent (C) is present covering the periphery of a capillary tuft, while other lesions are rounded (arrow) and represent filling up of entire capillary lumina by proteinaceous deposits. PAS-stain, 500 $\times$.

which have a large number of organelles* such as mitochondria, endoplasmic reticulum and ribosomes. These cells appear quite active and probably are responsible for the production of the hyalinoid matrix which lies between them. The thickening of the basement membrane proper is thought to be due to an increase in the production of chemically normal basement membrane material. To date there is no agreement as to what cell makes the basement membrane of the glomerular capillaries, although both the epithelial and the endothelial cell have been implicated. During the early stages of diabetic glomerulosclerosis, the diffuse form, the typical nodules are absent and the process is nondiagnostic. In fact, it is identical to the diffuse glomerulosclerosis of chronic glomerulonephritis or that produced by chronic liver disease.

Nodular Form

As the process continues, the diffuse form gradually becomes nodular. Nodules result from a slow and progressive increase in the amount of hyalinoid matrix and mesangial cells in the central region of each glomerular capillary tuft. Transition stages are frequently observed by both light and electron

microscopy, and there seems little doubt at this time that both diffuse and nodular glomerulosclerosis are stages of the same process. The typical nodule described by Kimmelstiel and Wilson in the diabetic kidney is composed of a core of interlacing bundles of hyalinoid matrix, among which are many mesangial cells and some nonspecific osmophilic debris. Usually the nodule is located peripherally in the glomerulus and is surrounded by open capillaries. The capillary basement membranes continue to thicken and may be two to five times the normal thickness by the time frequent nodules have developed.

Obliterative Stage

The third and most severe stage of diabetic glomerulosclerosis, the obliterative stage, has been observed more and more frequently in recent years, probably because of the better care and resulting longevity of diabetics. In this stage the nodules become quite large, often fusing, and compressing the peripheral capillaries until the capillary lumina are finally obliterated. Eventually, the glomerulus becomes completely ischemic and acellular. We refer to these glomeruli as the "large sclerotic glomeruli" to differentiate them from the "small sclerotic glomer-

*See Test Your Word Score Page 363.

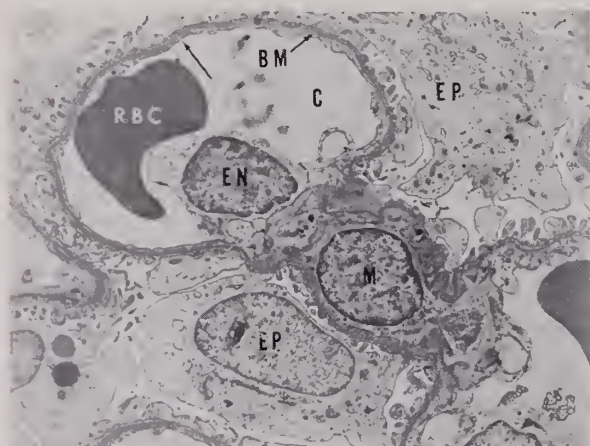


Fig. 6 — Electron micrograph of a portion of a normal glomerulus from a nondiabetic patient. One complete capillary loop (C) is present and contains a red blood cell (RBC). Near the mesangial area (M) there is an endothelial cell with nucleus (EN) which sends a very delicate band of fenestrated cytoplasm (arrow) around the inside of the basement membrane (BM). The basement membrane is covered externally by an epithelial cell (EP) with foot processes and intervening canaliculi. 2700X.

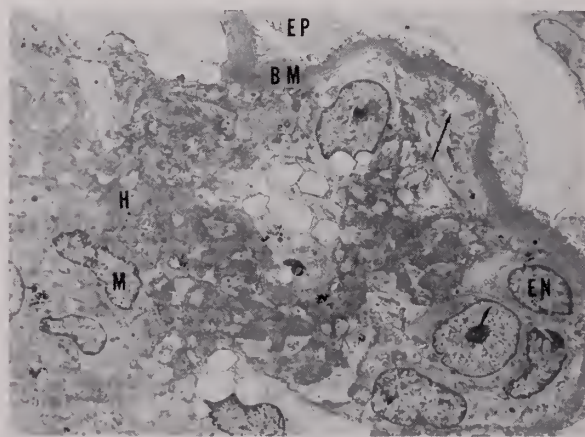


Fig. 7. — Electron micrograph of a portion of a Kimmelstiel-Wilson nodule in the glomerulus of a long-term diabetic patient. The nodule is composed of a markedly expanded mesangial area composed of mesangial cells (M) and interlacing bands of hyalinoid matrix (H). Peripheral capillary loops (arrow) are almost obliterated. Basement membrane (BM) is markedly thickened. Epithelial cells (EP) have lost much of their normal foot process structure. 1700X.

uli" of ischemic obsolescence and glomerulonephritis. In diabetes the obliterated glomerulus is quite large due to the massive deposition of hyalinoid matrix within the stretched basement membrane of the glomerular capillary tuft. Bowman's space is usually obliterated by enlargement of the capillary tufts, and adhesions are frequent between the parietal and visceral layers of the epithelial cells. The adhesions are more frequent in regions of exudative lesions to be described below.

Hypertension

Although statistics show that not all diabetics develop hypertension and, in fact, less than 50% of diabetics with microangiopathy have hypertension, in our experience almost all diabetics who progress to the stage of obliterative glomerulosclerosis and die in uremia have hypertension and its attendant body-wide arteriolar sclerosis. Therefore, in many cases of nodular glomerulosclerosis and in most cases of obliterative glomerulosclerosis, there is also severe hyaline arteriolar sclerosis in the kidney. As many as 30% of the glomeruli may undergo ischemic obsolescence due to the arteriolar occlusions.

Exudative Lesions

Exudative lesions are frequently found in association with the typical nodules of diabetic glomerulosclerosis and are especially frequent in the obliterative stage of glomerulosclerosis. These lesions have been given many names: "hyaline-fibrinoid", "crescents", "capsular drops", etc. We prefer the single term, exudative, since the lesions seem to be present more often in rapidly progressive, end-stage diabetic kidney disease and appear to be composed of plasma constituents with a high concentration of fibrin. In the light microscope, exudative lesions have a very homogeneous, glassy, eosinophilic, PAS-stain-positive appearance or may be vacuolated or foamy due to a high lipid content. They are found between the basement membrane and the endothelial cell, or they may completely fill some capillary loops. They may also cover the external surface of a capillary loop outside of the basement membrane and thereby assume a crescent

shape, or they may occur between the epithelial cells and basement membrane of the parietal layer of Bowman's capsule (capsular drops). Electron microscopy has demonstrated these lesions to be composed of a fine granular, osmiophilic debris which closely resembles the hyaline of the arterioles and the glomerular deposits of adult membranous glomerulonephritis and lupus.

We have found small deposits of similar black, granular material on both sides of the basement membrane of the glomerular capillaries of diabetics. This material has the appearance and location of the deposits of glomerulonephritis. We have postulated that in diabetes there is formation of a foreign protein which is trapped in the glomerulus

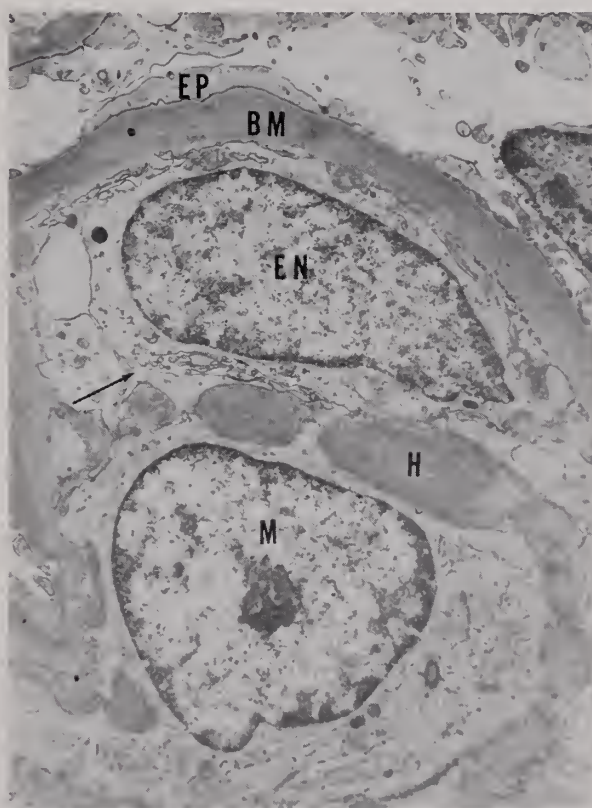


Fig. 8. — Higher magnification electron micrograph of a capillary loop from a long-term diabetic patient. The lumen (arrow) is almost obliterated and non-functional. Endothelial cell (EN) and mesangial cell (M) are shown. Note the concentration of organelles in the mesangial cell, indicating protein synthesis. Basement membrane (BM) is markedly thickened and the epithelial cell (EP) has completely lost its foot process structure. Note the marked thickening of the delicate mesangial matrix which, because of its pathologic nature, is labelled hyalinoid matrix (H). 7500 $\times$.

in very low quantities over a long period of time and that occasionally these proteins may accumulate rapidly and in large quantities to form the exudative lesions. It seems possible that these deposits represent the injurious agent which is stimulating the formation of excess mesangial cells and possibly the abnormal production of mesangial matrix. These thoughts are speculative and must be considered in the light of the fact that we may be dealing with a number of coincidental occurrences of diabetes and glomerulonephritis in the same patient.

The End Stage

The "end-stage kidney of diabetes" is a mixture of arteriosclerosis, nodular glomerulosclerosis, obliterative sclerosis of most glomeruli, arteriolar sclerosis with massive hyaline deposits in the walls of most arterioles, microinfarcts of individual nephrons with small sclerotic glomeruli of ischemic obsolescence and associated necrosis or atrophy of associated tubules, numerous glomerular exudative lesions and foci of pyelonephritis, acute and/or chronic.

Metabolism of Basement Membrane

At the present time most investigators believe that the key to diabetic glomerulosclerosis lies in an understanding of the metabolism of basement membrane and its related pathologic material, the hyalinoid matrix. Basement membrane is a glycoprotein with approximately 10% carbohydrate. It is generally believed that the pathologically thickened basement membrane and the

hyalinoid matrix are chemically similar to normal basement membrane and the mesangial matrix, but markedly increased in quantity. The quantitative increase in this material may be due to excessive formation or to decreased turnover. Both theories have adherents. Lazarow found an amino-acid composition similar to that of collagen and reported a decreased turnover.⁶ More recently, Spiro has reported some amino-acid differences between the basement membrane and collagen.⁷ His studies of the basement membrane carbohydrates reveal the presence of galactose, mannose and hexosamine. There are differences between the carbohydrates of basement membrane and the carbohydrates of the plasma glycoproteins which happen to be elevated in most diabetics. Thus, the possibility of a relationship between plasma glycoprotein metabolism and that of basement membrane seems remote. Until further information is available on glycoprotein metabolism and basement membrane chemistry, the problem of diabetic microangiopathy will probably remain unsolved.

Summary

Diabetic glomerulosclerosis is the renal component of diabetic microangiopathy. It begins as diffuse thickening of capillary basement membranes and proliferation of basement membrane-like material and cells in the mesangial area. Later nodules form and finally the glomerulus is obliterated. Intimal arteriosclerosis is severe and contributes to renal failure, which often supervenes.

References

1. Bloodworth, J. M. B., Jr.: Diabetic Microangiopathy. *Diabetes* 12:99, 1963.
2. Bloodworth, J. M. B., Jr.: Basic Similarities in Pathogenesis of Glomerulosclerosis Associated with Various Disease States. Presented to annual meeting of American Diabetic Association, New York, June 19, 1965.
3. Kimmelstiel, P. and Wilson, C.: Intercapillary Lesions in the Glomeruli of the Kidney. *Amer J Path* 12:83, 1936.
4. Kimmelstiel, P., Kim, O. J., and Beres, J.: Studies on Renal Biopsy Specimens with the Aid of the Electron Microscope. I. Glomeruli in Diabetes. *Amer J Clin Path* 38:270, 1962.
5. Aarseth, S.: Cardiovascular-Renal Disease in Diabetes Mellitus. *Acta Med Scand* 146 Suppl. 281, 1953.
6. Lazarow, A. and Speidel, E.: The Chemical Composition of the Glomerular Basement Membrane and its Relationship to the Production of Diabetic Complications. A chapter in: *Small Blood Vessel Involvement in Diabetes Mellitus*, ed. by M. D. Siperstein, A. R. Colwell, Sr. and K. Meyer, Amer Inst Biol Sci 1964.
7. Spiro, R. G.: Studies on the Structure of the Glomerular Basement Membrane. Presented to 26th annual meeting of American Diabetic Association, Chicago, June 25, 1966.

Fat Chances

Narrow minds fit small places.

Mediastinal Emphysema Complicating Acute Asthma

Report of Two Cases

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SPONTANEOUS DEVELOPMENT of mediastinal emphysema is a relatively rare complication of asthma that can be of grave concern and may even result in death. Herein reported are two examples of mediastinal emphysema complicating status asthmaticus and severe asthma with paroxysms of coughing.

Report of Cases

Case 1

A 29-year-old housewife was admitted to the hospital on March 3, 1966, in status asthmaticus. She had been asthmatic since seven years of age.

Physical examination revealed a dehydrated, dyspneic young woman with typical asthmatic wheezing. She had subcutaneous crepitation in the neck and a mediastinal crunch on auscultation.

Results of routine laboratory tests were normal except for eosinophilia of 10%. Results of acid-base studies by the Astrup method were within normal limits. A chest roentgenogram on admission showed mediastinal and subcutaneous emphysema (Figure 1).

The patient was treated with intravenously administered fluids, aminophylline, hydrocortisone sodium succinate (Solu-Cortef), Tedral, intermittent positive-pressure breathing with isoproterenol, and broad-spectrum antibiotics. She made a satisfactory recovery from the acute asthmatic attack, and only conservative treatment was necessary for the control of the mediastinal emphysema.

Case 2

A 19-year-old college student was admitted to the hospital December 27, 1965, with acute asthma. Two days before, she had experienced increasing difficulty with asthma, dyspnea, chest pain, vomiting, and severe coughing. She had a long history of asthma.

She had crepitation in the neck, axilla, anterior and posterior regions of the chest, and diminished breath sounds in the left base posteriorly. There were occasional inspiratory wheezing and sibilant rales.

Results of laboratory tests were within normal limits except for a 10% eosinophilia. Chest roentgenogram showed marked mediastinal and subcutaneous emphysema (Figure 2).

She was treated conservatively with prednisone, expectorants, bronchodilators, and high fluid intake and was asymptomatic when dismissed on January 6, 1966.

Discussion

Etiology

Payne and Geppert¹ in 1961 reported 32

*Mayo Clinic and Mayo Foundation: Section of Medicine.

cases from the literature. Either the condition must be a very rare complication of asthma or it is commonly overlooked.² It probably occurs more frequently than the medical literature indicates.³

Mediastinal and subcutaneous emphysema, associated with asthma, is believed to be due to an increase in intraalveolar pressure that causes rupture of alveoli adjacent to a bronchiole or pulmonary blood vessel. A forced expiration against a relative obstruction is generally necessary. Frequent increases in pressures as caused by coughing may also contribute. Air extravasates along the vascular sheaths and supporting tissues that extend to the mediastinum.

Air escapes into the subcutaneous tissues of the neck and down through the diaphragm into the retroperitoneal tissues, both areas acting as a safety-valve mechanism. Air may make its way forward over the heart, giving rise to a loud crunching sound (Hamman's sign) with each heart beat.⁴

Mediastinal emphysema from alveolar rupture occurs in adults with asthma, severe vomiting, labor and parturition, anesthesia, and violent coughing. A foreign body must

always be considered in a child. The same condition can occur from trauma with rupture of the lung, bronchi, trachea, or esophagus, and from carcinomatous involvement of the esophagus, trachea, or bronchi.

Diagnosis

Mediastinal emphysema can be recognized by a swelling and crepitation in the neck along with the mediastinal "crunch" on auscultation. The radiographic picture is characteristic. Air can be identified along the margins of the cardiac silhouette and adjacent to the pulmonary artery. The lateral chest radiograph is even more diagnostic (Figure 3) and shows air anterior to the heart, in front of the ascending aorta.⁵ Subcutaneous emphysema in the supraclavicular areas and in the region of the thoracic inlet was present in 13 of 16 cases.⁵ A lateral soft-tissue roentgenogram of the neck is helpful in identifying collections of air that have dissected upward into the neck along the paravertebral soft tissue.⁶

Prognosis

If a large amount of air is present, the



Fig. 1 — Typical pattern of mediastinal emphysema and subcutaneous emphysema apparent in the neck.



Fig. 2 — Mediastinal emphysema with subcutaneous emphysema of the neck, axilla, and anterior chest.

prognosis becomes more serious and surgical intervention should be considered. Death can occur from the pressure of air interfering with the return of blood to the right and the left atria, since the vena cava and pulmonary veins are thin-walled and have low pressures. Interference with venous return causes a low cardiac output, falling systolic and rising diastolic blood pressures, neck-vein distention, and finally cardiovascular collapse.⁷ Bilateral tension pneumothorax complicating mediastinal emphysema in asthma can cause death. A sudden critical increase in dyspnea associated with cyanosis, and pain confined to one side should direct suspicion to pneumothorax.^{8,9}

Treatment

The majority of patients should be treated conservatively. Cervical mediastinotomy¹⁰ may be necessary and, indeed, lifesaving if there is an indication of tension pneumomediastinum. Tracheostomy has been advocated by some¹¹ since it not only accomplishes mediastinal decompression but also decreases the intraalveolar pressure and affords a means by which secretions can be easily handled. Patients with tension pneumothorax are treated by surgical insertion of an intrathoracic tube and by water-seal drainage at negative pressures.

Intermittent positive-pressure breathing was administered to the first patient prior to recognition that she had mediastinal emphysema. Intermittent positive-pressure

breathing is contraindicated in patients with mediastinal emphysema and particularly where there is associated pneumothorax because of developing a tension pneumothorax and tension pneumomediastinum.



Fig. 3 — Lateral view shows air anterior to the heart, in front of ascending aorta, and in subcutaneous tissue of the anterior chest.

References

1. Payne, T. W., and Geppert, L. J.: Mediastinal and Subcutaneous Emphysema Complicating Bronchial Asthma in a Nine-Year-Old Male. *J Allerg* 32:135, 1961.
2. Gittelson, G., and Altman, D. H.: Pneumomediastinum as a Complication of Acute Bronchial Asthma. *J Florida Med Ass* 52:318, 1965.
3. Cooley, J. C., and Gillespie, J. B.: Mediastinal Emphysema: Pathogenesis and Management: Report of a Case. *Dis Chest* 49:104, 1966.
4. Hamman, L.: Spontaneous Mediastinal Emphysema. *Bull Hopkins Hosp* 64:1, 1939.
5. Ozonoff, M. B.: Pneumomediastinum Associated With Asthma and Pneumonia in Children. *Amer J Roentgen* 95:112, 1965.
6. Gay, B. B., Jr.: Radiologic Demonstration of Mediastinal Emphysema Complicating Asthma. *J Georgia Med Ass* 53:267, 1964.
- 7-11 May be secured from the author or the reprints.

Drive Safely

Being physically present and mentally absent is one of the greatest causes of accidents. — Charles Kettering

The Madstone*

In 1905 Dr. R. G. Curtin of Philadelphia was taking care of a case of hydrophobia which attracted considerable attention in the daily newspapers. He was soon in receipt of many letters from all parts of the United States offering the use of madstones.

The following is from a number of the Waco (Texas) Examiner as quoted in the Boston Journal of Chemistry (1879) :

"Dr. C. F. Groves, the druggist yesterday paid Mr. Weir of Brown County the round sum of \$250.00 for the stone reputed a veritable madstone. Mr. Weir we are told found the stone in a deer in Arizona County, and we are further informed that it never failed to extract the poison of mad dogs, snakes, tarantulas and other venomous reptiles, insects and animals. The doctor will keep the stone at his store for the benefit of any one who may wish to test its virtues."

And in the Charlotte (North Carolina) Observer, the following news item appeared :

"Mark Carroll, of Blacksburg, came to this City, yesterday and received treatment with the madstone at the office of H. M. Wilder, corner of Tryon and Third Streets. The stone stuck to him for a period of thirty minutes, Dr. Wilder reports."

The matter-of-fact fashion in which these reporters tell their stories, indicates that they must have believed them. Surely there is no evidence that they or the editors doubted them. Lest it be thought that such news items represent merely past convictions, the reader is asked to consider the following advertisement which appeared in the Warren County Times, of Tennessee, in the year of grace 1933 :

"We have a madstone guaranteed to give general satisfaction for mad dog bites and all poisonous bites. Has been applied to hundreds of bites and never lost a case. Reasonable price. Rev. R. J. Tucker, Summitville, Tenn."

*Thomen, A. A., M.D.: Don't Believe It! Says the Doctor. Blue Ribbon Books, New York, 1935.

Plants vs. The Human Species

In our dealing with plants nothing of a painful nature is encountered; no sad images are ever presented to our eyes; there is absolutely nothing to recall to our minds our passions, our disappointments, our misfortunes; love is never associated with jealousy, beauty exists without vanity, force is never accompanied by tyranny, and death takes place without agony; in brief, there is nothing to remind one of the human species.

— Frederic Cuvier (1773-1838)

Derivatively Speaking

Do you understand the difference in meaning and derivation between the two similar words, *pylephlebitis* and *pyelophlebitis*?

Pylephlebitis: inflammation of the portal vein — from the Greek *pyle* (gate) + *phleps* (vein) + *itis* (inflammation).

Pyelophlebitis: inflammation of the renal pelvic vein — from the Greek *pyelo* (pelvic) + *phleps* (vein) + *itis* (inflammation).

Arteriovenous Fistula

An
Unusual
Cause
of
Heart
Failure
in
an
Old
Man

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ARTERIOVENOUS FISTULA is a rare but curable cause of heart failure. This is a report on a 73-year-old man in whom spontaneous rupture of an arteriosclerotic left internal iliac artery aneurysm into the internal iliac vein resulted in high output heart failure. Surgical resection of the aneurysm and closure of the fistula, performed 20 years after the original diagnosis of the aneurysm and six years after the onset of congestive heart failure, resulted in dramatic improvement.

Case Report

A 73-year-old man was admitted to the hospital in March, 1966, because of increasing shortness of breath, orthopnea and ankle edema of three weeks' duration. A pulsating left-lower-quadrant abdominal mass had been present since 1946. At that time his blood pressure was 150/30 mm. Hg. and minimal cardiomegaly was noted on a chest x-ray film. He was free of symptoms and continued working until 1960, when he developed dyspnea and leg edema. Treatment with low-sodium diet, digitalis, rest, and diuretics resulted in prompt improvement, but subsequently he had repeated hospital admissions because of similar complaints. There was no history of back or abdominal pain, surgical operations, or traumatic abdominal injury.

Physical examination revealed an irregular pulse of 120 per minute; the blood pressure was 140/30 mm. Hg. The neck veins were pulsating and distended when the patient was sitting up. The cardiac apex was at the anterior axillary line. A grade 3, blowing, holosystolic murmur was heard maximally at the apex, also over the precordium and in the axilla. Crepitant rales and dullness were noted at the lung bases. A pulsating 8 × 4 cm. mass was palpable in the left-lower-quadrant of the abdomen and was also apparent on rectal examination. A thrill was present and a loud, continuous "machinery" murmur was audible over the aneurysm. The peripheral pulses were full and bounding. There was 2+ pretibial edema.

Generalized cardiomegaly and pulmonary vascular congestion were found on a chest x-ray film (Figure 1-a). An electrocardiogram revealed atrial fibrillation and increased voltage of the QRS complexes suggesting left ventricular hypertrophy. The urine sediment showed 80-90 red blood cells per high-

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power field. Right and transeptal left heart catheterizations were performed (Table 1). The results indicated biventricular failure, increased cardiac output and a large left-to-right shunt at the level of the bifurcation of the inferior vena cava. Minimal mitral regurgitation was observed on ciné left ventriculography. An aortogram demonstrated filling of a large aneurysm of the left internal iliac artery. Later films showed appearance of the contrast agent in the inferior vena cava (Figure 2). Dye dilution curves revealed an early and enlarged recirculation peak (Figure 3-a).

Surgical exploration revealed an aneurysmal dilatation of the left internal iliac artery. The artery was 8 cm. in diameter at its widest portion and tortuous, pushing the left common iliac and external iliac artery upwards and forwards. The terminal portion of the left common iliac artery was also involved in the aneurysmal process. Just inferior to the anterior rim of the true pelvis a

continuous bruit was palpable. Compression of the left internal iliac artery obliterated the bruit.

The internal iliac artery and the terminal portion of the left common iliac artery were excised and the aneurysm mobilized, but attempts to expose the actual communication with the vein were not pursued after an initial attempt because of excessive bleeding from multiple dilated and tortuous veins. Multiple deep suturing was done at the point of greatest bruit, and the internal iliac artery leading to and leaving the fistula was ligated and transected. A 10-mm. in diameter and 7-cm. long Dacron graft was inserted to bridge the defect between the common iliac and external iliac arteries.

Magnetic flow meter measurements of the common iliac artery flow before excision of the aneurysm were 1,440 cc./min., peak flow and 660 cc./min., mean flow. After excision of the aneurysm and closure of the fistula, the peak flow in the left common iliac artery was 780 cc./min. and the mean flow was 180 cc./min.

The removed specimen showed that the aneurysm was 11 cm. in length and 8 cm. in diameter and appeared arteriosclerotic. Following the operation, the blood pressure was 120/50 mm. Chest roentgenogram demonstrated a striking decrease in heart size (Figure 1-b). A repeat dye dilution curve showed a more normal contour (Figure 3-b). The subsequent postoperative course was entirely uneventful.

Discussion

Abdominal arteriovenous fistula may be caused by: rupture of an arterial aneurysm into an adjoining vein; a stab or gunshot wound; and operation for removal of herniated nucleus pulposus.¹ Internal iliac arteriovenous fistula related to trauma at childbirth has been reported in women.²

TABLE I
Cardiac Catheterization Data

Site	Pressure mm. Hg.	Site	O ₂ Content Vol %
LA	V = 30 M = 13	R. common iliac vein	8.2
LV	120/13	IVC bifurcation	11.7
PA	57/19 M = 30	IVC L4-5 interspace	14.1
RV	58/9	Mid-RA	12.4
RA	V = 15 M = 12	PA	13.5
		BA	15.3
Oxygen consumption = 204 ml/min.			
Cardiac output = 11.3 L/min.			
LA = Left atrium		RA = Right atrium	
LV = Left ventricle		IVC = Inferior vena cava	
PA = Pulmonary artery		BA = Brachial artery	
RV = Right ventricle		M = Mean	



Fig. 1 — a (left) Preoperative chest x-ray film, Cardiomegaly is apparent. b (right) Postoperative film demonstrates marked decrease in heart size.

Rupture of an arteriosclerotic abdominal aneurysm is a catastrophic event in the natural history of this disease, but if the rupture occurs into a venous channel, the patient may survive for a time before succumbing to the resultant congestive heart failure. In this group of patients, the hemodynamic burden of a large left-to-right shunt may be placed on a patient whose cardiac reserve has previously been limited by coronary arteriosclerosis. Most of these patients die within a few weeks or months unless successful surgical closure is performed.³ The prolonged survival of our patient is unusual.

The diagnosis of a fistula between an abdominal arterial aneurysm and vein is not difficult. The presence of a thrill and a continuous "machinery" murmur over the aneurysm, with a widened pulse pressure and signs of heart failure, are the important clinical features. Dye-dilution curves are helpful in the diagnosis and localization of the fistula, particularly if the curve can be changed to a normal contour by compression of the fistula.⁴ Cardiac catheterization and angiography provide confirmatory evidence, but these studies are probably not essential in a typical case. In our patient the studies were done to assess the amount of mitral regurgitation and to exclude the possibility of an intracardiac shunt.

Hematuria observed in our patient has also been reported in other patients with this type of fistula and presumably is caused by venous congestion of the bladder.⁵ A more serious complication of aorta-vena-caval fistula is renal shutdown which has been reported as a cause of death in some patients.⁶

The first successful repair of an abdominal aortic aneurysm-inferior-vena-cava fistula was performed by DeBakey in 1954.³ Salem found 18 similar cases in the English litera-

ture from 1955 to 1965, of which 15 were operated and 13 survived.⁷

Summary

Rupture of an arteriosclerotic aneurysm of the left internal iliac artery into the adjacent vein produced heart failure in an old man. Surgical resection of the aneurysm and closure of the fistula resulted in immediate improvement.

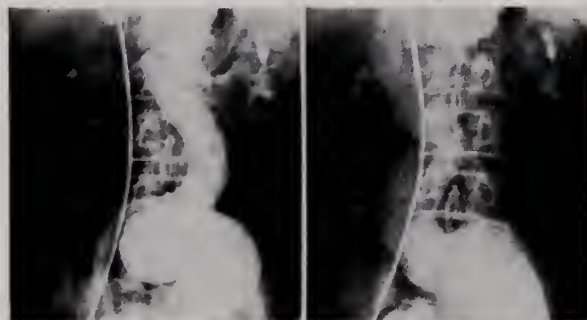


Fig. 2 — a (left). Aortogram demonstrates a large aneurysm of the left internal iliac artery. b (right) Later film shows appearance of contrast in the inferior vena cava.

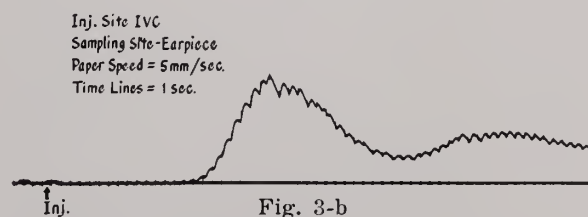
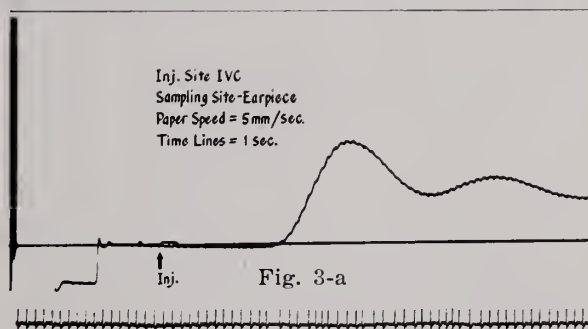


Fig. 3 — a (top). Preoperative dye curve. The early recirculation peak is suggestive of left-to-right shunt. b (bottom) Postoperative dye curve shows a normal recirculation peak.

References

1. Chiache, K., Tsuji, H. K., Schobinger, R., Kneisel, J. and Cooper, P.: Arteriovenous Fistula between the Common Iliac Vessels. Arch Surg (Chicago),

80:258, 1960.

2-7 May be secured from the author or the reprints.

Cook County Cervical Smear Clinic

THIS REPORT concerns the second annual "Pap Smear Clinic" sponsored by the Cook County Cancer Society. A highly successful effort by the Cancer Society, by volunteers, doctors, and public health officials of Cook County had resulted in the examination of 353 women during three clinics in April and May, 1965. Two carcinomas in situ were discovered, the women later obtaining curative treatment from their own physicians.

The same pre-registration techniques were followed after a "warm-up" publicity campaign. Practically the entire crew involved in this year's clinic were active in 1965 and the proceedings went smoothly throughout. Clinics were set for April 14, 22, 29 and May 6, 1966, with appointments at 10 minute intervals. This year only disposable supplies were used. A fee of \$4.00 was charged to cover costs of the special (reduced) fee charged by St. Luke's Hospital for reading the slides, and for supplies used. As before, all personnel involved donated their time and talents.

The information requested of each participant was slightly modified this year to conform to that requested by the A.A.G.P. form. All slides taken were sent to St. Luke's with the A.A.G.P. form; consequently each case automatically became part of the Academy's nationwide cancer detection project.

Results

A total of 373 women were examined and pap smears taken at the 1966 clinic. This figure is higher by 20 than the 1965 response. Only two women who were pregnant were seen at the clinic; the custom of not doing pap smears routinely on pregnant patients removes this segment of the population from clinic clientele.

Four cases of carcinoma in situ were discovered as a result of this clinic:

Clinic #	Age	Initial Pap Smear	Follow-up Pap Smear	Conization Report
101	42	Grade IV		CA in Situ
288	67	Grade IV		"
60	40	Grade II	Grade IV	"
135	36	Grade III	Grade IV	"

We found that 210 women who attended this clinic had been present at the first clinic.

A total of 163 women had their first pap smear this year. I found no obvious decrease in the number of office pap smears even during the month of the clinic itself. (I have kept track this year of the number of women seeking this test in my office, and also from Jan. 1st through Dec. 31, 1966, I have taken slides on 183 women). Thus the clinic approach does seem to reach a group of patients who are not ill and in whom a trip to the doctor's office for a pap smear tends to be postponed. It must be remembered that all four cases came from the "well" group of women, many of whom might not have bothered to see a doctor for the test.

The population of Cook county is about 3500 permanent residents. We estimate the adult female population at near 1,000 people. Thus 373 represents more than one third of the adult women. The additional 183 women seen in my office means that 556 women from this county have definitely had pap smears in 1966. In addition, it is certain a number of women will have had pap smears from the other physicians who see patients from Cook County.

Comments

It is my conviction, based on years of experience in dealing with enthusiastic volunteer lay groups helping in the conduct of "clinics," that community clinics offer the best, most inexpensive way devisable to apply mass screening programs of any type. The small town and rural communities in which I have practiced have never once failed to put over any such program suggested (i.e., cancer detection, immunization, tuberculosis testing). Our failure to help organize and participate in such programs costs people health and even life; participation repays a doctor with some of his most gratifying remuneration — the discovery that Medicine's "image" has grown just a bit less tarnished in the eyes of his fellow citizens. Undoubtedly mass community clinics will work better in small communities; however, an annual pap smear on over 50% of the adult female population of any community seems like a goal worth striving for.

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Editorials

Changes of Refraction and Diabetes Mellitus

SUDDEN AND often severe visual blurring frequently occurs as one of the more dramatic symptoms of diabetes. This blurring is due to an acute change in the refraction of the eye. This particular ocular change, while not so well known as the cataracts or retinopathy of diabetes, is of importance in that it may herald the onset of the disease or indicate poor control in an established case. Since Horner's original observation in 1873, much has been written about this subject. By 1925 Duke-Elder had collected 43 references from the medical literature. After the introduction of insulin, the refractive changes were observed even more frequently.

The essential features of the condition are the bilateral changes in refraction and their sudden appearance. An increase in the blood sugar causes a myopic change in the eye; conversely, a decrease in the concentration of sugar results in a hypermetropic change. The hypermetropic change does not occur as an initial phenomenon but follows a myopic change. The refraction commonly changes up to 2 or 3 diopters; Duke-Elder (1949) has recorded alterations ranging from -6 diopters to +9 diopters.

Initially, much speculation arose concerning the cause of these refractive changes, and many diverse theories to explain them appeared in the medical literature. Those dealing with changes in accommodation,

shortening or lengthening of the axis of the globe, changes in index of refraction of intraocular fluids, and changes in the corneal curvature have all been discarded on good evidence. By a process of elimination, plus the evidence reported by Elschnig in a case of unilateral aphakia* in which only the phakic eye showed the variations in refraction, the crystalline lens has become recognized as the site of changes producing alteration in refraction.

Three Theories

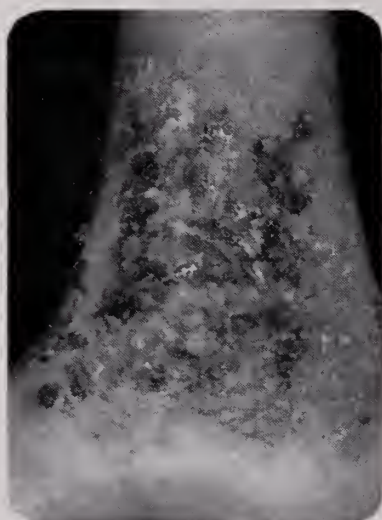
Although the lens is now agreed upon as the site, there is, by no means, agreement on the specific physical and chemical changes that account for the variation in refraction. Duke Elder (1949) states that three theories deserve mention: his own, that of Granström (1933), and that of Granström (1937), Bücklers, and Weekers.

Duke-Elder stated "... the myopia associated with a rising sugar concentration was due to hydration of the cortical layers of the lens relative to the nucleus. As the blood-sugar rises, provided the available water-reserve is maintained, the osmotic pressure of the aqueous tends to decrease, largely owing to the great elimination of osmotically active substances from the blood in the increased flow of relatively concentrated urine. The lens is a comparatively stable system, not readily participating in the fluctuations common to all the body fluids, and

*See Test Your Word Score Page 363.

Continued

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Administration and Dosage: Apply sparingly to the affected area 3 or 4 times daily. Some cases of psoriasis may be more effectively treated if the 0.1% Cream or Ointment is applied under an occlusive dressing.

Contraindications: Tuberculosis of the skin, herpes simplex, chicken pox and vaccinia.

Precautions and Side Effects: Do not use in the eyes or in the ear (if drum is perforated). A few individuals react unfavorably under certain conditions. If side

effects are encountered, the drug should be discontinued and appropriate measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive non-permeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyodermas will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

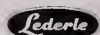
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therefore it will tend to maintain its original molecular concentration; consequently, in order to establish osmotic equilibrium, fluid tends to flow into it from the chambers of the eye. The lens therefore swells and is deformed, its curvature being increased; further, the optical density of its peripheral layers becomes diminished while the nucleus remains unaltered. On both counts its refractive power is increased, and the eye becomes myopic. If the inflow of fluid is rapid, actual droplets are formed under the capsule of such a size that they can be seen with the slit lamp, or even with the loupe; eventually a cataract may be formed, sometimes with great rapidity. Conversely, with a fall in sugar concentration, a reverse osmotic flow is inaugurated, and a condition of hypermetropia is produced."

Granström's 1933 hypothesis states that hydration of the nucleus of the lens is responsible for the hypermetropic change. He suggested that in hyperglycemia salt is retained in the tissues and, on diminution of the sugar, hydration follows. The lens shares in these changes, these phenomena being more significant in the nucleus, since the cortex attains rapid equilibrium with the aqueous.

Granström (1937), Bücklers (1939), and Weekers (1949) independently noted that reversible changes in the lens of a precatactous type occur in some diabetics. They concluded that the myopia was caused by an increased refractive index of the lens owing to changes of a precatactous nature caused

by a toxic agent; such changes are reversible and, on their amelioration, hypermetropia results.

Of these three theories, that of Duke-Elder is most widely accepted by ophthalmologists. However, no less an authority than Adler differs sharply with it. Instead of hydration of the lens he explained the myopia as due to dehydration and stated that when the osmotic pressure of the fluid bathing the lens rises, the lens becomes dehydrated with a so-called dry salt retention. With dehydration of the lens, its index of refraction rises, causing an increase in its dioptric power and resulting in a myopic change. On the other hand, if the osmotic pressure of the aqueous is lowered, water is retained in the lens and its refractive index drops, resulting in hyperopia.

From the foregoing one may conclude that although the lens is clearly implicated as the site for the change in refraction, no agreement has been reached on the actual chain of events occurring in the lens. Whatever the mechanism of these changes, a sudden and seemingly inexplicable myopia should always suggest the diagnosis of diabetes. Occasionally, in a known diabetic, it heralds a derangement in the control of the disease. In any case, treatment should not be directed toward the eye but rather toward the underlying metabolic disorder, for the change in refraction is transitory and invariably disappears when metabolic equilibrium is achieved.

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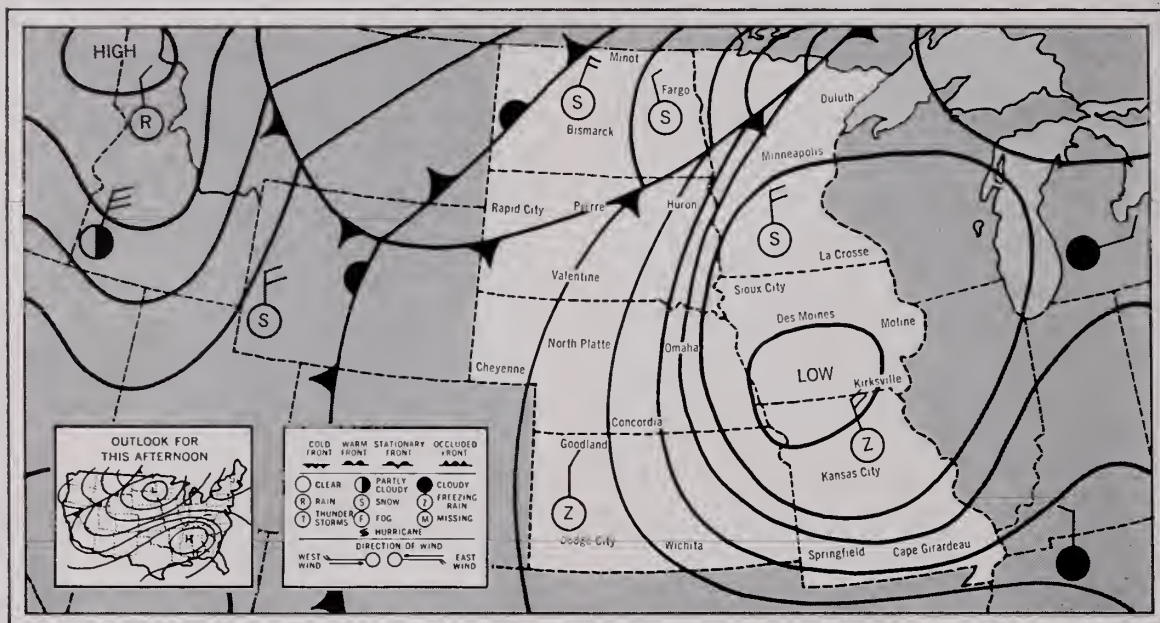
References

1. Adler, F. H.: *Physiology of the Eye: Clinical Application*. Ed. 4, St. Louis, C. V. Mosby Company, p. 889, 1965.
2. Bücklers, M.: *Zur Entstehung und Rückbildung des Zuckerstars*. *Klin Monatsbl Augenh* 102:465, 1939.
3. Duke-Elder, W. S.: *Changes in Refraction in Diabetes Mellitus*. *Brit J Ophthal* 9:167, 1925.
4. Duke-Elder, W. S.: *Text Book of Ophthalmology*. St. Louis, C. V. Mosby Company, Vol 4, 1949.
5. Duke-Elder, W. S.: *The Practice of Refraction*. Ed. 7, St. Louis, C. V. Mosby Company, p. 326, 1963.
6. Elschmig, A.: *Refraktionsänderungen bei Diabetes mellitus*. *Med Klin* 19:17, 1923.
7. Granström, K. O.: *Refraktionsveränderungen bei Diabetes Mellitus*. *Acta Ophthal* 11:1, 1933.
8. Granström, K. O.: *Transitory Cataract in Transitory Diabetic Hyperopia*. *Acta Ophthal* 15:523, 1937.
9. Horner: *Refraktionsänderungen*. *Klin Monatsbl Augenh* 11:488, 1873.
10. Weekers: Cited by Duke-Elder, W. D. (1949).

I wish Adam had died with all his ribs in his body. — Boucicault

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Diabetes and Pregnancy

THERE ARE no problems for physicians in general practice, internal medicine, pediatrics or obstetrics currently more challenging and involved than those presented by the diabetic, gravid woman. The price of neglect during management of the pregnant diabetic is high: permanent damage, or even death, for mother and child. It is proper and timely that MINNESOTA MEDICINE devote some attention to the progress already made, the present state of our knowledge, and the host of still unanswered questions in this area.

During the last 35 years, dramatic improvements have been documented over the morbidity and mortality figures of the pre-insulin era literature on the pregnant diabetic and her child. Nevertheless, many unhappy effects of pregnancy upon diabetes, of diabetes upon pregnancy, and of both upon the fetus remain poorly understood. Debated issues include such problems as how to diagnose more pre-diabetics; the best ways to test for diabetes mellitus during pregnancy; the mechanism whereby pregnancy unmasks the pre-diabetic; the causes of toxemia and hydramnios, which occur much more frequently in diabetic mothers; the good and bad influences of hundreds of agents, hormonal, nutritional, placental and external (such as medications); the best time and method for delivery; the roles played by insulin hyper-secretion and insulin-antagonists in producing alterations of maternal insulin requirement; and what precautions help avoid loss of the baby, or prevent later difficulty in its development. Doctor William N. Spellacy, whose comprehensive article appears elsewhere in this issue,* has participated in extensive researches into some of these questions.

It has been pointed out that the frequency and severity of fetal troubles seem related to the duration of the diabetes, and the severity of the vascular complications, in the mother. However in any individual pregnancy, no matter how mild or how advanced

the disease in the mother, the same distressing (and sometimes fatal) difficulties may be encountered in the baby: excessive size; frequent respiratory distress; congenital anomalies; hyaline membrane disease; evidence that physiologic maturity lags behind anatomic development; and proneness to develop diabetes mellitus. Death in utero contributes significantly to the present perinatal mortality of about 15 per cent. Infant problems are described in Doctor Spellacy's contribution, and emphasis is placed on the value of good diabetes control in the mother: i.e., the better the control of the diabetes, the better the perinatal survival statistics, and the fewer the congenital anomalies.

Does pregnancy cause diabetes? It seems to accelerate its appearance in some women whose tendency to become diabetic was not recognized. Pregnancy also causes some such women to appear diabetic according to certain tests during some part of the nine-month period, only to return to apparent complete normalcy after the pregnancy. These and similar observations have led to use of the term "Pregnancy Diabetes," which has meaning only if employed with the above information in mind. Diabetes-prone individuals may have clinically obvious diabetes appear as a result of any stress. If we use the term "Pregnancy Diabetes," why not "Surgery Diabetes," "Severe Trauma Diabetes" etc., knowing that these events may have only hastened the clinical appearance of the disease?

Brevity is the soul of wit¹ but also a source of misunderstanding. It is true that serial 24-hour quantitative measurements of urinary excretion of estriol may help in choosing the optimum time for delivery.* A simpler and more commonly available test is x-ray for fetal bone age. The statement "there is no evidence that pregnancy per se will change the ultimate prognosis or course of diabetes mellitus" needs qualification. Hagbard² studied 250 diabetic mothers and reported that six months post partum, 67 per cent showed no large change in insulin re-

*See page 329.

Continued

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quirement, 16 per cent required in excess of 12 units more for good regulation, and 17 per cent required more than 12 units less. These figures seem to cancel out statistically, but for each of the 83 diabetic mothers affected, the shift in insulin requirement of over 12 units can hardly be cited as evidence that pregnancy per se does not change the course of diabetes mellitus.

We may not wish to go to such lengths as does one Scandinavian clinic, which hospitalizes every diabetic mother twice during

pregnancy: briefly in the first trimester for strict regulation, then again from the thirty-second week until delivery. However, by using the team approach (general practitioner or internist and obstetrician and pediatrician) and requiring the strictest possible regulation of the pregnant patient's diabetes — based on present knowledge, we too can promise mother and child the best chance of a normal future.

E. B. Cohen, M.D.
Minneapolis, Minnesota

References

1. Shakespeare, W.: Hamlet, Act II, Scene 2, Line 90.
2. Hagbard, L.: Pregnancy and Diabetes Mellitus, in American Lecture Series Number 449, ed. by

Hamblen, E. C., Charles C. Thomas, Springfield, Illinois, 1961.

Insulin, Diet and Diabetes

IT HAS BEEN said that the discovery of insulin set back research in diabetes by at least twenty-five years. Everyone became preoccupied with the problems of treatment rather than the causes of the ailment. When the sulfonylureas were discovered thirty-five years later we still had no knowledge of the cause of diabetes mellitus.

Concern with the presence of sugar in the urine has led to recognition that at least two sugars other than glucose may be present without real diabetes mellitus being present. The same concern with glycosuria has certainly blinded us to the far-reaching disturbances that characterize diabetes mellitus. It seems that we measure the amounts of glucose in the blood and the urine because we are too ignorant to measure anything else.

Forty-five years after the discovery of insulin, we still do not have criteria for the diagnosis of diabetes mellitus. Not only do we not have figures for the normal glucose values in persons over fifty years of age, but there is even a question of how diagnostic the glucose tolerance curve may be in persons under fifty.

Dr. Bloodworth* has summarized the basement membrane changes in renal capillaries in diabetic nephropathy, but what is

the significance of the same changes in the child of diabetic parents who has not yet shown changes in glucose metabolism? Is he a diabetic or even a pre-diabetic; or is he only a histologic curiosity?

Perhaps no disease state outside of the general field of neoplastic disease or the problems of aging has been so intensely studied in its superficial or peripheral manifestations without having its basic defects or causative factors defined.

The objective in the day-to-day control of diabetes mellitus is primarily the maintenance of a state of normoglycemia. This is generally accomplished by the use of insulin and the periodic determination of the blood-sugar level or the extent of glycosuria.

We should not overlook, however, a fundamental contribution to the science of diabetic management by a man who was not a physician but a biochemist. The name of Somogyi is usually associated with the method of determining the true glucose content of the serum; however, he proposed a still more useful concept that has been too long unappreciated; namely, the concept of glucose utilization as an index of adequacy of control: a consideration more important, we believe, than concern for the amount of glucose lost in the urine. The proposed ideal in dietary and insulin management of diabetes

Continued

*See page 335.

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Marks, V., and Dawson, A.:
Brit. M. J. 7:293, 1965.

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should be the highest ratio between the amount of glucose utilized in grams per day and the units of insulin required each day. Rather than raising the insulin dose to cover the glucose lost, Somogyi proposed that the glucose ingested might be lowered in order to avoid excessive wastage. Certain British clinics currently achieve this end by pre-

scribing only the carbohydrate limitations in the diabetic diet, leaving the protein and fat to find their own levels, depending on the patient's needs and appetite. This is really the essence of practicality in diet prescription.

Philip H. Soucheray, M.D.
St. Paul, Minnesota

Prevention of Neonatal Death*

IT IS TRAGIC to admit, but statistically valid, that — despite our most sophisticated techniques of treatment for the Rh-sensitized pregnancy — there still remains an 8% to 10% neonatal death rate in such cases. The present forms of therapy reveal their inadequacy in several stages of the approach.

Initially, if every pregnant woman is not screened for irregular antibodies other than ABO and D, hemolytic disease may become manifest when least expected. Typing for other factors in the Rh system and in other blood groups need be done only if screening of the mother's serum demonstrates an irregular antibody. The test cells for screening should contain all red-cell antigens likely to cause hemolytic disease. Irregular antibodies known to cause hemolytic disease generally belong to the incomplete immune globulins.

Secondly, when positive titers and amniotic-fluid densities forewarn of impending disaster, we cannot accurately forecast fetal ripeness; for there is as yet no reliable method of determining fetal maturity, especially when one is operating purposely close to the grey zone of immaturity. Parenthetically, too many amniocenteses are still being performed without attempts having been made to locate the placenta. Placental tissue transgressed by needle puncture transports fetal cells into the maternal circulation, thereby exaggerating an already critical situation by introducing additional antigens riding on fetal cells into the maternal system.

Lastly, intraperitoneal fetal transfusion must be regarded as a formidable procedure carrying with it both fetal and maternal

morbidity and perhaps mortality. Although teams of trained individuals frequently exposed to the variables of the procedure can minimize complications, additional reports of difficulties undoubtedly will appear in our obstetric literature.

More effort must be directed to our most recent approach to the problem: namely, prevention rather than detection and therapy. At present we administer high-titer anti-Rh globulin to the immediate-post-partum Rh-negative woman whose ABO system is compatible with that of her husband. The rationale for administration of the anti-Rh γ -globulin is based on the original findings of Theobald Smith who demonstrated in 1909 that neutralized mixtures of diphtheria toxin and antitoxin containing an excess of antitoxin did not immunize when injected. If a specific antibody is administered passively to an individual, subsequent injections of the corresponding antigen will usually fail to sensitize. However, the level of the passively administered antibody must be sufficient to maintain an excess at all times.

Before final evaluations can be written regarding the procedure, we must continue to improve methods for quantitating minor populations of fetal red cells in the maternal circulation and maintain a close follow-up of patients who have received the γ -globulin throughout several pregnancies. Efforts thus made may ascertain when sensitization actually occurs in a particular pregnancy, with perhaps future use of anti-globulins during pregnancies in which sensitization would ultimately occur.

Edward A. Banner, M.D.
Rochester, Minnesota

*Adcock, L. L.: Erythroblastosis Fetalis: Management at the University of Minnesota Hospitals. 49:1081, 1966.

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The following is a brief precautionary statement. Before prescribing, the physician should be familiar with the complete prescribing information in SK&F literature or *PDR*. **Contraindications:** Comatose states or the presence of large amounts of C.N.S. depressants. **Precautions:** Potentiation of C.N.S. depressants may occur (reduce dosage of C.N.S. depressants when used concomitantly). Antiemetic effect may mask other conditions. Possibility of drowsiness should be borne in mind for patients who drive cars, etc. In pregnancy, use only when necessary to the welfare of the patient. **Side Effects:** Occasionally transitory drowsiness; dry mouth; nasal congestion; constipation; amenorrhea; mild fever; hypotensive effects, sometimes severe with

I.M. administration; epinephrine effects may be reversed; dermatological reactions; parkinsonism-like symptoms on high dosage (in rare instances, may persist); weight gain; miosis; lactation and moderate breast engorgement (in females on high dosages); and less frequently cholestatic jaundice. Side effects occurring rarely include: mydriasis; agranulocytosis; skin pigmentation, lenticular and corneal deposits (after prolonged substantial dosages).

For a comprehensive presentation of 'Thorazine' prescribing information and side effects reported with phenothiazine derivatives, please refer to SK&F literature or *PDR*.

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Arterial Injuries

THAT ARTERIAL injuries demand prompt attention is an accepted surgical principle. An important article by John J. Bergan, M.D., appearing in the September issue,* points out the fact that iatrogenic arterial injuries are no different from those caused by trauma of any other kind.

There exists in every physician a reluctance to accept the fact that he has, through his action, caused harm to his patient. The physician must hurdle this emotional barrier before he can properly diagnose and treat iatrogenic arterial injury; but if he has disciplined himself to "stand apart" and view the problem objectively, little time will be lost because of his emotional involvement.

Dr. Bergan discusses arterial injuries occurring in the operating room. These may become less common or at least be more adequately handled in the future, since graduates of most approved surgical training programs now acquire a substantial exposure to vascular surgical techniques. He points out, however, that diagnostic procedures which necessitate arterial puncture now constitute the most common cause of iatrogenic arterial injury. More and more of these procedures are being performed by persons without appreciable surgical

training, such as the cardiologist and the radiologist. It does not seem practical that these diagnosticians should train themselves as vascular surgeons. They must, however, be willing to function as clinicians and draw appropriate conclusions from the patient's symptoms and the findings of physical examination. This will be a new experience for the radiologist, but will, I believe, make his work more exciting.

To make his procedure as safe as possible the diagnostician should see and evaluate his patient beforehand. He should adopt a schedule of pre-medication that will sedate the patient properly (the most important factor in the successful performance of a local anesthetic procedure). He must follow and examine his patient after the procedure for at least 24 hours. He must discipline himself to accept the signs of arterial injury and promptly seek help from the vascular surgeon when indicated. He should consider avoiding such procedures if vascular surgical help is not available in his community. Then the arterial injuries which are inevitably incurred in the performance of such diagnostic procedures will be handled with the least morbidity and best possible result.

Frank E. Johnson, M.D.
Minneapolis, Minnesota

*See Bergan, John J.: Iatrogenic Arterial Injuries. *Minnesota Med* 49:1375, 1966.

Abdominal Arteriovenous Fistulas and Congestive Heart Failure

IN THIS ISSUE* there is a case report of "an unusual cause of heart failure" by David A. Berman and colleagues. This interesting case deserves further comment. An abdominal arteriovenous fistula is certainly an uncommon cause of congestive heart failure, but its recognition is important because of the potentially curable nature of the lesion. Recently I had two patients with this problem. Although the correct diagnosis was made within two weeks after the rupture of

the aneurysm, in each instance the outcome was jeopardized by the lapse of time after the formation of the fistula.

Review of the Mayo Clinic files back to 1919 revealed five cases of aortocaval or iliovenous fistula. All were associated with congestive heart failure—one with chronic failure such as reported by Berman and co-workers. It should be emphasized, however, that abdominal aortocaval fistulas usually cause large left-to-right shunts and, subsequently, acute high-output cardiac failure.

Continued

*See page 345.

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1. Schleif, R.H.: J.A.P.H.A., 46:179, 1957 *U.S. Pat. No. 3,062,714

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Repair was successful in one of the five cases from this institution; in this case a clot occluded the lumen of the fistula. Perhaps clotting in the fistulous tract is associated with a longer survival, such as in the case reported by Berman and co-workers. The abdominal aortic aneurysm may be small and not palpable, but certain clues on examination of the heart and pulses should alert the clinician to listen carefully over the abdomen and lower part of the back for the diagnostic bruit. The bruit may or may not be continuous. The bounding carotid pulse with a wide pulse pressure in the absence of a murmur of aortic insufficiency strongly suggests rapid runoff through a peripheral arteriovenous fistula. Central fistulas of the lungs are not associated with these findings. Signs of right heart failure secondary to venous overloading are found in the acute cases of heart failure. These findings include a right ventricular lift on palpation, with marked increase of the jugular venous pressure. A large V wave with a holosystolic murmur at the left sternal border suggests the presence of tricuspid insufficiency. Mitral insufficiency may be present because of dilatation of the mitral annulus.

In one of our cases, the patient presented with severe venous insufficiency of the right lower extremity. The leg was blue and markedly edematous, but the pulses were intact.

In addition, rupture of the abdominal aortic aneurysm into the inferior vena cava can simulate acute low back pain from a ruptured intervertebral disk. Indeed, the fistula

may result from surgical trauma in the removal of such a disk.

A thoracic roentgenogram usually is not helpful except to exclude the presence of a thoracic aneurysm. Shortly after the formation of the fistula, the electrocardiogram may indicate right ventricular strain with a shift in the frontal axis to the right. Special procedures such as cardiac catheterization are not absolutely necessary and may be contraindicated in a severely ill patient. Although thoracic and abdominal aortograms may be occasionally helpful in localizing the fistula, often they are not because of the rapid runoff through the tract. The clinical picture of congestive failure, bounding peripheral pulses, warm extremities, and a continuous abdominal bruit is sufficient evidence to warrant abdominal exploration without special procedures.

One final note is about the use of digitalis in patients with arteriovenous fistula and congestive heart failure. The drug should be administered with caution. It is likely to be less effective than when given for low-output congestive failure. Cardiac arrest occurred postoperatively in one of our patients. He had been digitalized rapidly in the 24 hours prior to the operation, and repair of the fistula caused a sudden, profound diuresis. In retrospect, perhaps rapid shifting of the electrolytes and potassium excretion predisposed this patient to severe digitalis intoxication.

Carlos E. Harrison, Jr., M.D.
Rochester, Minnesota

Surgery on the Extracranial Vessels

THE ARTICLE by Garamella, et al.* in the November issue of MINNESOTA MEDICINE adds to the growing literature on the subject of surgery directed towards the extracranial blood vessels. They summed up the problems inherent in this subject when they stated, "Admittedly, the functional results are more difficult to evaluate than anatomical corrections made, and long term studies

are necessary for further elucidation." In short, the restoration of blood flow in a vessel cannot be equated with the return of function of the nervous tissues supplied by this vessel.

The natural history of arteriosclerosis of the carotid and vertebral arteries is not completely known and further information on this subject is urgently needed. There is ample evidence that complete or partial occlusions of the extracranial vessels may be present without interference with cerebral

Continued

*Garamella, J. J., Lynch, M. F., Jensen, N. K., Sterns, L. P., and Schmidt, W. R.: Extracranial Internal Carotid Artery — Surgery for the Totally Occluded. *Minnesota Med* 49:1669, 1966.

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True enough, it doesn't. The closest hospitals to Apache Plaza Medical Complex are from 9 to 15 minutes away. But then again, we must remember . . . over 95 per cent of a doctor's patients do not require hospitalization. By relocating adjacent to a hospital, you might put a geographic imposition on your patients, as well as your previous hospital commitments.

Doctor . . . as a matter of fact, Apache Plaza is the center of the community for all of northwest St. Paul, northeast Minneapolis, and suburbs.

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function.^{1,2,3,4} The collateral circulation is sufficient to avoid any functional impairment.

Another serious question to be answered is the role of surgery and anticoagulant therapy vs. no therapy in this group of patients. Control studies are necessary in which comparable patients are divided into three groups: those who receive no treatment; those who receive anticoagulant treatment, and those who have repair of the involved vessels.

In order to be able to assess the results of surgery directed towards the extracranial vessels, careful study of the patient's status prior to and subsequent to surgery is indi-

cated. In this area, the majority of general surgeons are of necessity dependent upon evaluation of the status of the cardiovascular and nervous systems by consultants, as they themselves are not particularly trained in diseases of the brain and cardiovascular systems. Only by careful documentation prior to and subsequent to surgery of the patient's functional status can any reasonable conclusions be drawn; therefore a team effort directed towards this evaluation is to be encouraged.

The field of surgery on the extracranial vessels is in its infancy. Far more experience is necessary before any final conclusions can be drawn as to the efficacy of surgery and the indications for it.

*Clinical Professor of Psychiatry and Neurology, University of Minnesota.

Sidney K. Shapiro, M.D.*
Minneapolis, Minnesota

References

1. Gurdjian, E. S. et al.: Completed Stroke Due to Occlusive Cerebrovascular System. *Arch Neurol* 7:545, 1962.
2. Millikan, C. H.: Perplexities in Cerebrovascular Disease. *Ann Intern Med* 58:191, 1963.
3. Fazekas, J. S.: Prognostic Uncertainties in Cerebrovascular Disease. *Ann Intern Med* 58:93, 1963.
4. Moossy, J.: Personal Communication.

Test Your Word Score

Rinderpest — *cattle plague — from German rinder: cattle + pest: plague (page 314).*

Alloxan — *a urea which tends to destroy the islet cells of the pancreas (page 332).*

Good King Henry — *an herb of the Chenopodium family, such as pigweed (page 333).*

Venus' looking-glass — *an herb of the species Campanula (page 333).*

Osmium tetroxide — *a crystalline compound used for staining histologic preparations (page 335).*

Organelles — *one of the minute organs of protozoa concerned in the functions of metabolism, etc. (page 338).*

Aphakia — *congenital absence of the lens of the eye (page 349).*

Syringomyelia — *a condition marked by abnormal cavities filled with liquid in the substance of the spinal cord (page 385).*

Shwartzman phenomenon — *a severe hemorrhagic reaction with necrosis (page 410).*

Voyageurs — *those who travel by stream, portaging between streams with their canoes and supplies on their backs (page 435).*

Riches

The man who dies rich dies disgraced. — Andrew Carnegie

what time is it?

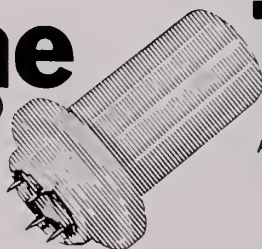
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You May Be Right

"Only 53 cases have been reported in the English literature."

What is meant by the term "English literature?" Is it to be differentiated from Scottish or Irish journals; or is it to include American journals?

It seems that the word English when used as an adjective still carries a sense of pertaining to England. One would hardly expect to find the writings of Mark Twain in a college course of English literature. However, few of us consider that we talk American but rather English, regardless of whether we are natives of Jamaica, Hong Kong, Cork, or Los Angeles. It seems that when we want to express the fact that we have abstracted articles written in the English language we had best refer to them as papers in English rather than English literature.

So, in this instance where most of the cases had been reported in American journals, "only 53 cases have been reported in English" is to be preferred.

Raymond C. Read, M.D.
Little Rock, Arkansas

The Editor's Soliloquy

"I've Got You Down for a Thousand"

It was late March and the income tax deadline was imminent. Our accountant, an enthusiastic Disabled American Veterans advocate, had come over to examine the books. Together we analyzed almost everything: our income and outgo, our profits and losses, and the numerous possible deductions for this and that, some of which were acceptable, others not. Contributions to the church, civic opera, art museum, community fund and various minor charities, as well as auto, convention, and entertainment expenses if incurred for business purposes: all these were deductible.

But not the paint job on the garage door, the lawn fertilizer, the snow removal, the frozen radiator, the installation of a picture window, the addition of a balcony, etc.

I was vicariously gratified, however, to learn that *if* I were a professional band director the initial cost and subsequent upkeep of my uniform would be deductible. Also my equine expenses, were I vocationally engaged in breeding and selling race horses.

Finally, when we had completed our examination and were relaxing with a cup of coffee to finish off the evening, a sudden after-thought shattered my complacency.

"Just one more thing, Doctor. The D.A.V.! Those boys in the blue caps and jackets — on the street corners — with slotted tin cups — and forget-me-nots! Whatever you contributed is deductible, you know. You may as well include it. How much was it?"

"Ten cents."

"WHAT!"

"Well, would you settle for a dollar?"

— Carl O. Rice, M.D.

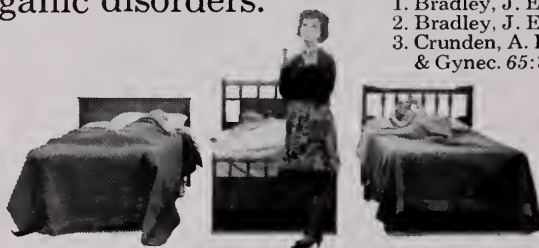
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1. Bradley, J. E., *et al.*: J. Pediat. 38:41 (Jan.) 1951.
2. Bradley, J. E.: Mod. Med. 20:71 (Oct. 15) 1952.
3. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. 65:311 (Feb.) 1953.



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Miss Gertrude M. Gilman

Miss Gertrude M. Gilman, Director of the University of Minnesota Hospitals, is one of the few woman administrators of a big university teaching hospital in the country. Her achievements and contributions are impossible to measure, as she has pursued her career in such a quiet, dignified manner that the impact of her influence is impossible to calculate.

She was born in Benson, Minnesota. Her father, Ira C. Gilman, came from Sioux Falls, South Dakota, and her mother, Minnie Neason Gilman, from Blockley, England. She has one brother, Neason Gilman, now living in Florida. Her father died in 1913 and her mother in 1947.

Continued

Miss Gilman graduated from the University of Minnesota in 1921. She planned to become a teacher but began work in the University Hospitals shortly after graduation from college and never left. Her personnel records show a steady progression through many positions to the Director of the Hospitals and Professor of Hospital Administration.

Through the years she has had a strong influence in molding the Hospitals' programs and in developing warm personal relationships with the physicians of the state, County Commissioners and directors of social agencies. Her professional career parallels the development of welfare programs from direct contact with probate judges, County Commissioners, County Welfare Departments, and Social Security up to the present Medical Assistance and Medicare.

She has had a part in the development of the institution from a small building of 120 beds to a great complex of 830 beds and a staff of almost 2,000. When Miss Gilman began as the Director of the Admissions Department, only the poor, the most indigent came for care. The same institution she now directs takes care of people of all financial circumstances who come from all parts of the world to receive help.

One of the important points in her career probably came when Mr. Ray Amberg was appointed director of the outpatient department in 1929. At that time the Eustis addition and the Out Patient Clinic building were attached to the Hospital and made one institution. Miss Gilman became the Admission Director for the Clinics as well as for the Hospitals. This early recognition of her abilities and expansion of her functions brought her directly into policy-making and administration. This also was the beginning of a long association and close working relationship with Mr. Amberg.

The Director of Admissions holds one of the most important positions in a medical setting. The income of the institution, the relationships with physicians, community leaders, patients and other interested people all depend upon the manner in which this position is filled. Mr. Amberg, Director of the Hospitals, established liberal policies which Miss Gilman carried out. He believed sick people should be helped whenever they were in need of the services the University Hospitals and Clinics could provide. Each specific situation was reviewed and the attempt made to extend the services of the institution to patients and physicians. Miss Gilman was particularly adept in establishing a warm bond of friendship with physicians practicing in all parts of the state. Many she knew as students and internes and they were accustomed to her being in a position to be helpful to them.

Influence on Teaching Program

The Out Patient Clinics were considered an essential adjunct to the teaching program of the Medical School. Mr. Amberg and Miss Gilman believed the interests of medical education could best be served by liberal admission policies to encourage doctors, agencies and patients to use the services. In this way the clinics were able to provide a wide scope of medical conditions and diseases to enhance the teaching program and facilitate the students' learning experience. This was a most difficult course to follow in those early days and required great tact and diplomacy.

Physicians often accused the University of taking business away from private doctors or of providing medical care for people who could afford to pay physicians' fees. The financing of medical care had to be authorized by the County Commissioner of the patient's legal settlement. This required tact and great ability to interpret the medical needs and the responsibility for providing medical care. Miss Gilman's diplomacy, patience and gentle manner were most successful in these areas. If this function had not been so thoughtfully carried out, the Hospitals would not so easily have been able to change the groups served and become an institution predominantly serving patients who pay their own expenses. One of Miss Gilman's greatest contributions was the excellent relationships she was able to build with all groups: patients, physicians and the general public.

Coordinating Department Heads

Of all the administrators, Dr. Louis Baldwin, Mr. Paul Fessler, Dr. Hulbert Dunn and Mr. Ray Amberg, under whom Miss Gilman worked, Mr. Amberg had the greatest influence on her career. Her advancements parallel his; as he was promoted, he increased her areas of responsibility. It is not often that a hospital is so fortunate in having a pair of administrators who work so well together and complement the talents of each other so completely. Mr. Amberg believed that department heads should run their own departments as independently as could be allowed within the structure of his administration. As much help as was needed was available and that help often came from Miss Gilman. After the opening of the Mayo addition in 1956, the institution became a large formal operation. Miss Gilman was able to assume the responsibilities for the management of the Hospital, leaving Mr. Amberg free to make a tremendous contribution to the American Hospital Association as its President, to participate in lobbying important health and welfare legislation through the Congress, and to build a firm foundation for the institution in Minnesota.

Everyone on the staff of a teaching institution has an obligation to participate in the educational program. The University Hospitals, as a part of a great University, has taken a position of leadership in training personnel essential to medical care. The various departments carry out full teaching programs and are themselves similar to small colleges. Dietetic Department, Medical Technology, X-Ray Technicians and the five schools under the Department of Physical Medicine are all lodged in the hospitals and under the direction of the staff assigned to direct the departments. Other departments of the University send students to the Hospitals for training, e.g., Schools of Hospital Administration, Pharmacy, Dentistry, etc.

A Program of Hospital Administration

Miss Gilman's contribution to the program of Hospital Administration is certainly one of the greatest of her career. While she has indisputably achieved recognition in administration, her influence as an educator deserves equal merit. The students whom she directed through their year of

Continued

internship acquired her compassion for people and her devotion to patient care. They learned the art as well as the technique of administration. Many of the students she has taught over the past years now hold important positions throughout the country. Miss Gilman has participated directly in all the other areas of the Hospitals' teaching program through special lectures and conferences.

Genteel Dignity

In reviewing such a steady, successful career, particularly in such a masculine and competitive field, it is essential to attempt to distinguish those personality factors which have influenced, if not produced, such a remarkable career. To those who have known and worked with her over the years Miss Gilman presents many outstanding personal attributes. The most obvious is her genteel dignity. She is quiet, a lady in the true sense and always in command of herself and the situation in which she happens to be. She is an excellent executive and gets her points across in a mature way without the need for undue emotion. She is a humble person, sensitive to the needs of others, and a person of genuine integrity. All through her career, in every position, her focus has been on patients. She has never let her responsibilities for the development of programs, administrative structures or policies deflect her concern for people. If she was ambitious for herself, no one ever sensed it. Each promotion she seemed to meet with surprise and simple gratitude. She never pushed or jockeyed for position but rose to the top on pure merit.

In her dealings with staff and personnel she is always fair and understanding. She is able to translate her feelings and opinions most directly in a manner which leaves little room for misunderstanding, but she does so in a genteel manner, sensitive to the feelings and objectives of her staff.

Another of Miss Gilman's attributes which has contributed to her success is her phenomenal memory. She seldom forgets a name, a face, or a situation. Many people with excellent memories can recall unusual events, but she can remember both unusual and ordinary, a marvelous asset for a Hospital Administrator, as this allows her to keep thousands of facts in mind.

Organizational Activities

Miss Gilman has participated in the activities of many professional organizations. She served as a member of the Committee on Nursing, Liaison Committee of the National League of Nursing, American Hospital Association, Steering Committee of the Minnesota League for Nursing, and Chairman Administrative Practices Committee and Twin City Regional Hospital Council, President's Report 1958-60.

She also served as a member of the Committee on Nursing of the American Hospital Association, Hospital Nursing Service Liaison Committee, Advisory Committee of Study to Project Future Needs for Nursing in Hospitals, Committee on Nursing Service and Education in National Defense, Committee on Careers of the National League for Nursing, Joint Committee of the American Hospital Association and American Dietetic Association, trustee of the Twin City Regional Hos-

pital Council, member of the Chaplaincy Committee Greater Minneapolis Council of Churches, and member of the Health Committee of the Community Health and Welfare Council of Hennepin County.

Miss Gilman's has been a professional life of sincere devotion to the Hospitals. Though this has been her consuming interest, she has still been able to achieve a balance between professional and personal life, a unique achievement. Her interests outside of her job have been the simple relaxing pleasures of most women — family, home, travel, and friends.

Miss Gilman has a home and garden at 4209 Aldrich Avenue South. Miss Ione Corliss, for many years Director of Nursing for the Out Patient Department, lives with her. Miss Gilman takes frequent trips to Florida to visit her brother and his family and has made several trips to England to visit relatives and her mother's home community.

Her life at the University of Minnesota Hospitals is characterized by devotion to the task of providing medical care to people. That devotion has been emulated by her students and staff. Her influence has been extensive and thousands of people live happier, more satisfactory lives because of her 42 years of dedicated efforts in their behalf.

Annie Laurie Baker
Minneapolis, Minnesota

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Curbstone Consultation

Pleural Effusion

QUESTION: I have a 24-year-old male patient who developed a left pleural effusion. Repeated cultures of the serous colored fluid have failed to demonstrate any bacterial growth. The chest X ray is negative so far as any pulmonary parenchymal lesion is concerned. He has a positive tuberculin test, but no acid-fast bacilli have been found on several gastric analyses. A pleural biopsy has not been performed. Would you recommend tuberculous antibacterial therapy in this man, particularly in the face of the chest X-ray findings?

ANSWER: A large number, perhaps even a majority, of patients with tuberculous pleurisy with effusion will develop active tuberculosis in some part of the body within five years. In the great majority of cases, tuberculosis is the cause of so-called idiopathic pleurisy with effusion among patients possessing positive tuberculin tests. For this reason, in the case cited, the patient certainly deserves an antibacterial therapy regimen directed against tuberculosis. Such a regimen should ordinarily extend over at least a continuous 18-month period. Although isoniazid alone is probably adequate, some physicians prefer to combine its use with aminosalicylic acid. You relate that a pleural biopsy was not done. The diagnosis may often be made through use of that procedure when other diagnostic measures have failed. Therefore, utilization of that diagnostic technique should be seriously considered before initiating the program of chemotherapy.

Harold D. Kletschka, M.D.
Assistant Professor of Surgery
State University of New York
Syracuse, New York

*Why, if the Soul can fling the Dust aside,
And naked on the Air of Heaven ride,
Were't not a Shame — were't not a Shame for him
In this clay carcase crippled to abide? — Omar Khayyam (?-1123)*

*One age cannot be completely understood if all the others are not understood.
The song of history can only be sung as a whole. — Ortega Y Gasset*

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The Viewing Box

THIS IS A nine-year-old male whose pertinent history began three days prior to his admission to Children's Hospital. At that time there was an abrupt onset of diarrhea and generalized crampy abdominal pain. This was followed the next morning by intermittent vomiting. Because of persistence of the vomiting and the diffuse abdominal pain, the patient was seen by his family physician who gave the child Thorazine, with abrupt cessation of vomiting. However, the patient continued to have diffuse abdominal pain, and on the day of his admission the pain became somewhat more severe and localized. Throughout this three-day history it was noted that the patient had a persistent temperature of around 101 degrees orally.

On physical examination, rebound tenderness was noted throughout the abdomen. Exquisite tenderness was noted in the retrocecal area.

Laboratory findings revealed a leukocyte count of 29,950 with 90 per cent neutrophils. The hemoglobin was 13.9 grams and the urine contained occasional red blood cells per high power field.

X-ray examination of the chest was negative (Figure 1). The abdominal film revealed a moderate reflex ileus and a 1-cm. laminated right pelvic calcification.

What is your diagnosis? (See next page.)



Fig. 1 — Supine abdomen taken on admission to hospital. It shows ileus and a 1-cm. laminated right pelvic calcification.

DIAGNOSIS: At surgery, an acute, gangrenous appendicitis with rupture and periappendiceal abscess was found. The appendix contained a 9×15 mm. coprolith, which is well shown on an x-ray of the specimen (Figure 2).



Fig. 2 — X-ray of removed appendix. Note bulbous distention distal to coprolith.

Coproliths

Coprolith is a word derived from the Greek, meaning "dung stone". In general it refers to a fecalith which contains sufficient calcium phosphate to make it radiopaque. Appendiceal calculi (or coproliths) are radiographically demonstrable in from four to fifteen percent of the patients with acute appendicitis. In the genesis of a coprolith, impairment of the normal fecal return from the appendix into the cecum results in the formation of an inspissated appendiceal fecalith. The combination of mechanical irritation by the fecalith and the bacterial activity produces a low grade catarrhal inflammation, resulting in formation of a large amount of mucus. The inorganic salts in the mucus (chiefly calcium phosphate) are precipitated on the surface of the fecalith, transforming it into a radiopaque coprolith. Repeated episodes result in lamination and enlargement of the coprolith with additional "inflammation" in the adjacent appendiceal wall.

Because of the variation in the position of the appendix, the coprolith may be found anywhere in the right abdomen, and rarely on the left side. However, in the vast majority of cases, it is found in the right lower quadrant, usually at the level of the sacroiliac joint or iliac crest. In most instances, it is laminated; occasionally it is faceted, especially when multiple stones are present. It is usually round or oval and commonly under 2 cm. in size. In approximately two thirds of reported cases, only a single stone is visualized.

Acute appendicitis is the most common abdominal disease requiring surgery, and it is estimated to be the cause of 17,000 deaths annually in the United States. Recognition of a coprolith may lead to an earlier diagnosis of acute appendicitis, particularly in those cases which are atypical or whose signs and symptoms suggest another condition.

Acute appendicitis is present in 90 percent of patients with coprolith formation, and in 50 percent of such cases perforation has already occurred. In many patients with coprolith formation, the history, physical and laboratory findings are atypical of appendicitis and the diagnosis may

COPROLITHS

not be suspected unless an abdominal film is taken. Therefore, while an abdominal film is unnecessary in clinically typical cases of appendicitis, it should be taken in any case of atypical abdominal pain. Radiological demonstration of a coprolith should prompt immediate exploration despite the atypicality of the signs and symptoms of acute appendicitis clinically.

Occasionally patients with coproliths and without symptoms are encountered. These patients almost invariably develop acute appendicitis subsequently; therefore in such patients, prophylactic appendectomy is probably indicated.

Conditions which can simulate coproliths include benign bone islands, ureteral and vesical calculi, calcified mesenteric nodes, phleboliths, radio-paque medication, gallstones, and calcified appendices epiploiae. While any of these can offer diagnostic difficulty, appropriate x-ray studies will usually differentiate.

A typical case of acute appendicitis with a coprolith is presented. In making the correct diagnosis and initiating prompt therapy in atypical cases, however, the recognition of a coprolith is important and can be made only by an abdominal film.

John O. Judge, M.D.
Charles T. Miller Hospital
St. Paul, Minnesota

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Sound horn when passing.

Take special care when passing trucks. Trucks may appear to be going more slowly than they are.

Check to see if drivers ahead or behind are going to pass. Check traffic conditions around you. Check side and rear view mirrors.

Stay in the passing lane until you can see the car you've passed in your rear view mirror. Signal before moving back into the right-hand lane.

Adjust speed to traffic flow. Avoid zig-zagging from lane to lane to pass other vehicles.

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Benjamin Franklin 1706-1790

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Tumor Conference

Tumor and Tuberculosis

AN APPRECIATION of the higher incidence of carcinoma of the lung in patients with tuberculosis has emerged in the last decade. A recent case pointed up this relationship and raised other problems in diagnosis and management which are worthy of comment.

Case Report

The patient was a 45-year-old barber and janitor who was admitted to the respiratory isolation ward on 10-1-64 with a fever and a cough after x-ray examination of his chest showed multiple nodular densities with cavitation in both upper lung fields. He was an alcohol addict. He had been treated in the outpatient department for mild diabetes managed by diet and oral hypoglycemic agents. He had smoked one to two packages of cigarettes a day for 30 years. In the ten years preceding admission he had been hospitalized or treated for "pneumonia" on eight occasions in various parts of the country.

The admission sputum cultures grew out typical *mycobacterium tuberculosis*. On subsequent testing these organisms were sensitive, *in vitro*, to para aminosalicylic acid, isoniazide and viomycin. The patient was intensively treated for six months in the hospital with isoniazide and para-aminosalicylic acid. He was discharged after marked resolution of the pulmonary infiltrates and after six sputum cultures showed



Fig. 1 — This chest film shows the right upper lobe mass, indicated by the arrow.

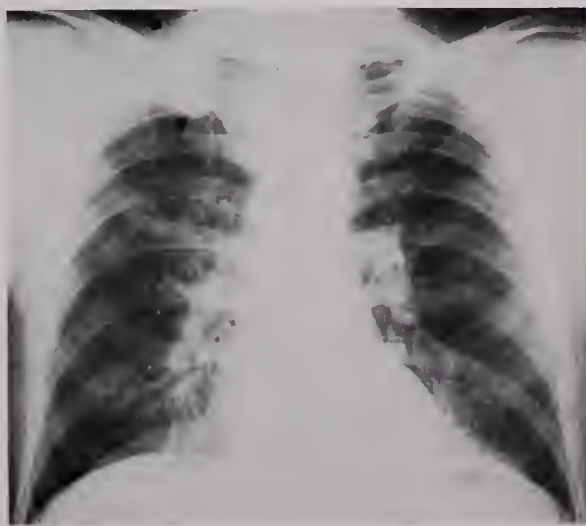


Fig. 2 — The upper arrow indicates the area of destruction of the second rib. The mass is slightly larger than on the film three weeks previously.

Continued

TUMOR CONFERENCE

no growth of *Mycobacterium*. He was followed with serial roentgenograms and cultures in the outpatient department while continuing on medications. One year after his original admission he was admitted for a second time because one of the follow-up cultures grew *M. tuberculosis*. Shortly after this second admission, he complained of mild right shoulder and chest pain. Admission chest films showed some increase in the infiltrates in the right apex.

The admission film is shown in Figure 1. In comparison to the films of the preceding two months there was no change in the nodular lesion in the right upper chest. During the next two to three weeks the patient complained of more chest pain and pain with motion of the right shoulder. Because of this, a chest film was taken (Figure 2) and destruction of the right second rib was noted. A planigram (Figure 3) illustrates the rib erosion better. Preoperative studies showed a hemoglobin of 12 gm., wbc. 9,700, with 47% PMNs, 34% lymphocytes, 4% monocytes, 14% eosinophils, and 1% basophils. VDRL was negative. BUN was 14 mgm.%. FBS was 126 mgm.%. A 2-hour p.c. blood sugar was 309 mgm.%. A BSP test had 4% retention at 45 minutes. Bence-Jones proteins were not present in the urine. One-second forced expiratory volume was 2.3 liters; 3-second forced expiratory volume was 3.5 liters. There were no significant findings on bronchoscopy. Scalene lymph node biopsy did not contain tumor in the nodes obtained.



Fig. 3 — This is a planigram showing the rib erosion between the two arrows.

On 4-11-66 a right thoracotomy was done. The tumor was found to be adherent to the second and third ribs. The spinal column, azygos vein, and vena cava were not involved. The right upper lobe was resected in continuity with the first, second, third and fourth ribs and transverse processes. Grossly, the tumor had not invaded locally beyond the chest wall. Examination of the specimen showed a well differentiated peripheral bronchogenic squamous cell carcinoma invading the chest wall. The hilar nodes were free of tumor but showed caseous necrosis. Postoperatively, the patient was continued on isoniazide and para-aminosalicylic acid. There were no operative complications. The shoulder pain did not recur. Unfortunately, two months postoperatively, severe left back pain occurred. X rays showed a destructive lesion in the left scapula. Local therapeutic x-ray treatment was started in hopes of giving pain relief. Within several weeks other metastases appeared in the dorsal and lumbar spine as well as the right scapula. The patient had increasing debilitation with wasting. He died four months postoperatively. Autopsy confirmed the presence of widespread metastatic squamous cell carcinoma.

Comment

Although this case could be dismissed as the simple chronicle of an unfortunate patient dying of uncontrolled bronchogenic carcinoma of the

lung, it does raise several interesting questions. First, is there any important relationship between carcinoma of the lung and pulmonary tuberculosis? In our hospital there appears to be more than a fortuitous relationship of the two diseases. Between 1947 and 1965 there were 1164 new cases of carcinoma of the lung admitted to the Minneapolis Veterans Hospital.¹ Of these, 43 patients (about 4%) had been treated or were under treatment for tuberculosis. Other authors, reviewing recent experience, have quoted an incidence of association of the two diseases varying from 2 to 9% in the United States² to as high as 31% in countries with high tuberculosis infections rates.³ Most of the studies supporting the idea that tuberculosis increases the likelihood of bronchogenic carcinoma have been in the last ten years since the introduction of effective antituberculosis agents. In the past, "tuberculosis was the disease of the young who did not live to see the cancer age."⁴ White, Beck and Pecora⁶ emphasized the changing age of the tuberculosis patient. In a New York State Sanatorium, in 1940, men over 45 years old represented only 5.9% of the population. By 1957, over 40% of their patients were men over 45 years old. It is only reasonable to assume that patients with advanced tuberculosis are surviving longer since the advent of antituberculosis drugs. Steinitz³ used the excellent disease registries for tuberculosis and cancer in Israel to get a better estimate of the risk of bronchogenic carcinoma occurring in patients with active or inactive tuberculosis. She made an extensive study of these patients who appeared in both registries. It was her conclusion that having tuberculosis increased the risk of developing bronchogenic carcinoma over that of the general population by a factor of five in males, and by a factor of ten in females. Incidentally, less than 2% of the women were smokers. In other series, where smokers are much more frequent, the additional effect of heavy smoking is not clear.

The evidence is fairly clear that the finding of *Mycobacterium* in the sputum of a patient with pulmonary disease should make the possibility of malignancy *more* rather than *less* suspect. A patient who has tuberculosis has a risk of developing carcinoma of the lung equal to that of a heavy smoker.³ In several series, the diagnosis of cancer was made in tuberculosis patients by the usual means. In 15 patients, Holden⁵ found gross tumor by bronchoscopy in four. Six of seven patients, who had sputum smears examined, had tumor cells present. One of eight patients had a positive scalene node biopsy.

In the case presented above, the occurrence of rib erosions pointed clearly to malignancy. Less blatant signs of possible cancer are: (1) Clearing of pulmonary infiltrates in one area of the lung during therapy while disease is progressing in another area; (2) X-ray evidence of progression of the disease with a persistently negative sputum; (3) Unilateral hilar enlargement; (4) Progressively enlarging nodular densities arising during treatment; (5) Persistent expiratory rhonchus. If diagnostic tests remain negative for tumor and strong suspicion of tumor is present, a diagnostic thoracotomy should be performed.

The site of bronchogenic carcinoma is not necessarily in physical relationship to the tuberculous infiltrates or old scar. White, Beck and Pecora found that the carcinoma occurred in the areas of previous tuberculosis in only one half of their cases.⁶

Continued

TUMOR CONFERENCE

The second question raised by the unhappy outcome in this patient was whether the extensive curative attempt was worth while in the face of chest-wall invasion. At the Minneapolis Veterans Hospital, in-continuity chest wall resection for tumor invasion has been done on 20 (6.5%) of 306 cases resected in a curative attempt between 1947 and 1965. Most of the cases were done in the past five years. Of those patients in whom there is a follow-up, six of 11 possible patients have survived for one year, and one of five possible patients has survived from those patients done at least three years ago. It would seem from this brief experience that the attempt is worthwhile. This is confirmed by Grillo⁷ who had three of 19 patients having in-continuity lung and chest wall resections surviving four to 14 years. The results are similar to the series by Gronqvist, Clagett, and McDonald,⁸ who had four of 16 possible patients surviving one year to six and a half years.

Grillo's findings further emphasized the necessity of chest wall resection rather than extrapleural dissection.⁷ None of his 14 patients treated by extrapleural resection survived over four years compared to the three survivors with chest wall resections.

As a third and final point, it should be emphasized that chest wall and/or shoulder pain with any pulmonary lesion is highly suspicious of malignancy⁹ and is the most common symptom of chest wall involvement.⁷ Clagett found this symptom in 14 of his 16 resected cases.⁸

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References

1. Humphrey, E. W., Rao, K., and Van Nostrand, D.: Current Therapy of Carcinoma of the Lung. Progress in Clinical Cancer, Irving M. Ariel, Editor. 2:253, 1966.
2. Allen, A. R. and Allen, L. M.: The Appearance of Carcinoma of the Lung in Pulmonary Tuberculosis Patients. S Dakota J Med 19:13, 1966.
3. Steinitz, Ruth: Pulmonary Tuberculosis and Carcinoma of the Lung. A Survey from Two Population-Based Disease Registers. Amer Rev Resp Dis 92:758, 1965.
4. Bender, F.: Primary Pulmonary Carcinoma Associated with Active Pulmonary Tuberculosis. Dis Chest 21:184, 1952.
5. Holden, H. M., Quilan, J. J., Hiltz, J. E.: Coexisting Pulmonary Tuberculosis and Bronchogenic Carcinoma. Canad Med Ass J 93:1306, 1965.
6. White, F. C., Beck, F. and Pecora, D. V.: Co-Existing Primary Lung Carcinoma and Pulmonary Tuberculosis. Amer Rev Tuberculosis 79:134, 1959.
7. Grillo, H. C., Greenberg, J. J. and Wilkins, E. W.: Resection of Bronchogenic Carcinoma Involving the Thoracic Wall. J Thorac Cardio Surg 51:417, 1966.
8. Gronqvist, Y. K. J., Clagett, O. T., and MacDonald, J. R.: Involvement of the Thoracic Wall in Bronchogenic Carcinoma. J Thorac Cardio Surg 33:487, 1957.
9. Engelman, R. M.: Shoulder Pain as a Presenting Complaint in Upper Lobe Bronchogenic Carcinoma: Report of 21 Cases. Conn Med 30:273, 1966.

All silencing of discussion is an assumption of infallibility and, as all history teaches, neither communities nor individuals are infallible. — John Stuart Mill

One finger in the throat and one in the rectum make a good diagnostician. — Osler

Medical Seminar

Tick Paralysis

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TICK PARALYSIS is a rapidly fatal but easily cured disease of man and animal, produced by the bite of a tick and characterized by an ascending symmetric, flaccid paralysis. This disease is distinct from the tick-borne rickettsial diseases.

William Hovell¹ in 1824 was the first to report this disease when, while travelling through Australia, he noted that a small insect called a tick "buries itself in the flesh and would in time destroy either man or beast if not removed in time." Initially, tick paralysis was a problem only for sheep herders, who annually lost many of their sheep to this condition. (Numerous ticks were found fastened to the backs of the sheep.) The occurrence of tick paralysis in North America was not noted in the literature until 1912 when Todd² reported cases involving persons from British Columbia; these cases dated back to 1898. Since that time additional reports of tick paralysis in both man and animal have appeared in the literature, describing further the clinical and the pathophysiologic aspects of this disease.

Incidence

As of 1965, about 100 cases have been reported in the United States. The mortality rate in these cases is about 10%.³ In Canada, the 250 cases reported to date have had a mortality rate of 11.2%.³

Although seen in adults, the disease is more common in infants and small children; twice as many girls as boys are involved. The higher incidence of girls is attributed to

their having longer hair which provides an optimal situation for the tick to remain implanted and undetected.

Tick paralysis has been seen in 15 of the 50 states but is common only in states west of the Rocky Mountains (Washington, Oregon, Idaho, Montana, Colorado, and Wyoming) and in British Columbia and Alberta, Canada. In Australia the regions with the highest incidence are situated in two narrow strips along both eastern and western coasts.

The Vector

The tick *Dermacentor andersoni* is largely responsible for the cases in the Pacific Northwest; the *Dermacentor variabilis*, for those from eastern and southern United States; the *Amblyomma americanum*, for those from southern United States; and *Ixodes holocyclus*, for those from Australia. In the state of Minnesota, *D. variabilis* seems to be a prominent species.⁴ However, there are no reports of paralysis in Minnesota being caused by this species. Briefly, the wood tick passes through four stages of development: egg, larva, nymph, and adult.

Egg, Larva Stage

The eggs are laid in masses in thick clumps of grass. After they are hatched, the larval forms attach to host animals (usually small rodents), become engorged with blood, and drop to the ground. On the ground they shed their skin and become nymphs.

Continued

The Nymph and Adult Stage

The nymphs then attach to another host, again engorge themselves with blood, and in several days drop to the ground, molt, and become adults. The adults of both sexes are next brushed from the grass or shrubs onto a passing host (man or animal).

The Host

They may immediately fasten themselves via their mouthparts to the host and, as is more commonly seen, migrate from the lower extremities upward toward the head. This migration has given the false impression that the ticks have fallen from trees.

In choosing its final point of attachment, the tick favors a protected region of the body. It attaches to the scalp or neck area in 63%⁵ of the cases and in the remainder, to areas such as the inguinal and axillary regions, the vulva, and the umbilicus. Once attached, the ticks mate or engorge themselves with blood from the host or do both. Complete engorgement requires six to 10 days, during which time eggs develop in the female and both male and female may increase in weight from 1 to 450 mg. Maximal engorgement occurs between the third and the fifth day. The adults then drop off, and the female lays her eggs and dies.

The Neurotoxin

Production and injection of the neurotoxin responsible for tick paralysis requires at least four to six days of engorgement. Such a long latent period between attachment and paralysis is extremely important epidemiologically, as a patient may have the disease and be well outside the endemic area. Although the majority of cases are caused by the female tick, a few cases⁶ attributable to males have been reported recently.

In general, ticks attach in early spring and summer. In temperate climates they are rarely seen after August 1.

Clinical Aspects

The classic clinical picture is seen in a child or infant and, as stated previously, more commonly in a girl.

Non-specific Complaints

Twelve to 24 hours prior to paralysis, the patient may manifest vague, nonspecific complaints such as irritability, fatigue, paresthesia in the lower extremities, and fleeting muscular pains.

Weakness

The child often appears well when put to bed in the evening, but on arising in the morning is noted to have weakness in the lower extremities and a prominent ataxia in all upper and lower extremities. It is uncertain whether this ataxia is cerebellar in origin or secondary to the weakness per se.

Flaccid Paralysis

During the next few hours, the weakness changes to a flaccid paralysis. Twelve to 48 hours later, this paralysis progresses from the lower extremities to the upper ones in a rather symmetric fashion and, if the tick is not found and removed, the progression continues to eventually involve the cranial nerves in the same ascending symmetric manner. There may be sternocleidomastoid paralysis, lingual paralysis, dysphagia, dysarthria, facial paralysis, and ocular weakness.

Respiratory Paralysis

Eventually the patient dies of respiratory paralysis unless the causative tick is found. Respiratory paralysis may occur suddenly and unexpectedly, and its threat must always be anticipated. Myoclonic twitches and choreiform movements have been reported to occur during the earlier stages. Convulsions may occur terminally and are believed to be secondary to hypoxia.

Physical Findings

On examination, the prominent finding is a flaccid paralysis of the extremities associated with decreased or absent deep-tendon reflexes. Early in the course there may be a positive Romberg sign along with dyssynergia and dysmetria in the upper extremities. Sensory signs usually are absent, although sensory symptoms such as pain and par-

esthesia are frequently noted. Evidence of cranial-nerve palsies such as ptosis, as well as facial and palatal weakness, may be present. The general sensorium and mood of the patient characteristically remain normal, although apprehension often appears terminally. Temperature and pulse also remain normal unless bulbar involvement occurs or unless an infectious process is also present.

Unusual instances of localized weakness occur. Examples of these are facial weakness from a tick in the external auditory canal, frontalis and orbiculares oculi paralysis from a tick on the forehead, leg weakness secondary to a tick on the genitalia, and brachial-plexus palsy associated with a tick over the brachial plexus.

Laboratory Findings

The cerebrospinal fluid is characteristically normal, although occasionally the pressure may be slightly elevated; the serum protein may reach 50 mg. per 100 ml., and a slight pleocytosis may exist. Results of routine blood studies are normal in most cases.

Prognosis

The course of tick paralysis depends entirely on two factors: when the tick is found and whether it is removed. If the tick is removed early, there may be no symptoms at all. If it is removed during the illness and prior to bulbar weakness, improvement invariably occurs within hours and ability to walk returns 12 hours to two days later. Complete recovery by one week is the rule. If the tick is allowed to remain until bulbar symptoms have begun, death will often occur from respiratory paralysis despite heroic measures.

Differential Diagnosis

Polio is the most frequent consideration in the differential diagnosis. However, there are several features that distinguish polio from tick paralysis: In contrast to polio, patients with tick paralysis have no fever, no meningeal signs, no muscle spasms, and

a normal spinal fluid. Guillain-Barré syndrome, tumor of the cord, and syringomyelia* can be differentiated because of the normal results of the sensory examination and the normal spinal fluid seen in tick paralysis.

Pathologic Features

In general, pathologic studies are unrevealing. In one case⁷ in which the diagnosis of tick paralysis was doubtful, the patient had diffuse cerebral engorgement and round-cell infiltration. In the experimental animal, pathologic alterations are inconsistently seen and, when present, include congestion in the brain as well as in the anterior and posterior horn grey matter of the spinal cord.

Neurotoxin

Origin

Experimentally, paralytic symptoms have been produced only with gravid females or ripening eggs. Emulsions of salivary glands from the female tick injected subcutaneously into mice produce paralysis, but do so in a rather inconsistent manner. Thus, it is doubtful whether salivary glands alone are responsible for the disease. Emulsions of the eggs of the tick also produce the disease in experimental animals and apparently with greater frequency than do emulsions of either the salivary gland or the whole tick. At present, both the salivary glands and the eggs are believed to contain the neurotoxin. The neurotoxin apparently is injected into the host via the salivary-gland secretions of the tick.

Site of Action

The site of action of the neurotoxin has been described recently by Murnaghan.^{8,9} Neurophysiologic studies were carried out on dogs paralyzed by *D. andersoni*. The anterior tibial muscle was isolated for study and was noted to contract normally on direct stimulation but not to contract when stimulated via the peroneal nerve. Subsequent stimulation of the ventral root produced a normal action potential at several sites along the nerve, thus indicating that

*See Test Your Word Score Page 363.

Continued

those parts of the nerve were normal. Repetitive stimulation of the nerve indicated that the paralysis was unlike that noted with neuromuscular blocking agents but was more suggestive of an abnormality in the tiny terminals of the nerve. Subsequent studies on the same preparation revealed no abnormality of acetylcholine synthesis or storage but showed a decreased release of acetylcholine from the nerve terminal after stimulation. Thus, Murnaghan^{8,9} concluded that the site of block was at the tiny, pre-synaptic terminal fibers of the somatic motor nerves.

Treatment

The first step in successful treatment is the clinician's suspicion of this disease in instances of ascending paralysis that occur between February and August. A careful search for the tick must be made, the clinician taking care to examine the preferred sites of attachment. Once located, the tick must be carefully and completely removed, because only after the head parts are removed will the symptoms clear. Several

methods of removal have been suggested: (1) A volatile substance such as ether, gasoline, or kerosene may be spread over the tick; (2) a lighted cigarette or match may be placed near the tick; (3) petrolatum may be used to cover the tick; and (4) adhesive tape may be placed over the tick and pulled gently.

With each of these measures, five to 10 minutes are required for the tick to loosen its grip. Once the tick is removed, the wound should be treated with a germicidal agent. Because infection can result, crushing the tick between the fingers must not be attempted. To kill the tick, kerosene or turpentine should be used.

Anti-tick dog serum has been tried in animals with moderate success. However, use of such sera in humans has resulted in severe urticarial reactions.

In cases of bulbar paralysis, adequate support of both respiration and blood pressure is important.

Narcotics should be avoided in view of the threat of respiratory depression.

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Rochester, Minnesota

References

1. Hovell, W. H.: Cited by Abbott, K. H.: Tick Paralysis: A Review. I. *Proc Mayo Clin* 18:39; 59, 1943.
2. Todd, J. L.: Does a Human Tick-Borne Disease Exist in British Columbia? *Canad Med Ass J* 2:686, 1912.
3. Epidemiologic Notes and Reports: Death Associated With Tick Paralysis. In: *Morbidity and Mortality Weekly Report*. Atlanta, Georgia, U. S. Department of Health, Education, and Welfare, Public Health Service, Sept. 18, 1965, vol. 14, p. 319.
4. Cutkomp, L. K.: Minnesota Ticks and Their Control. University of Minnesota Agriculture Extension Service, U. S. Department of Agriculture, St. Paul, Minnesota, Fact Sheet no. 27, May, 1964.
5. Rose, I. (Kamloops, B. C.): Review of Tick Paralysis. *Canad Med Ass J* 70:175, 1954.
6. Henderson, F. W.: Tick Paralysis: Report of a Case in Florida. *JAMA* 175:615, 1961.
7. Stanbury, J. B., and Huyck, J. H.: Tick Paralysis: A Critical Review. *Medicine* 24:219, 1945.
8. Murnaghan, M. F.: Site and Mechanism of Tick Paralysis. *Science* 131:418, 1960.
9. Murnaghan, M. F.: Conduction Block of Terminal Somatic Motor Fibers in Tick Paralysis. *Canad J Biochem Physiol* 38:287, 1960.

Every living body exhibits in a fourfold form the process of equilibration; from moment to moment in the balancing of mechanical forces; from hour to hour in the balancing of functions; from year to year in the changes of state that compensate changes of conditions; and, finally, in the complete arrest of vital movements at death.

— Herbert Spencer



Clinical Path Conference

Unusual Renal Complications in Diabetes Mellitus

A 69-year-old white male diabetic, was admitted to Hennepin County General Hospital because of fever and lethargy.

Eighteen years previously diabetes mellitus had been detected. Fifteen years previously insulin PZI, 15 units, regular 10 units) in addition to diet was necessary for adequate diabetic control. Routine laboratory tests at this time were normal.

The patient returned 14 years before his final admission because of nocturia (4×) and slowing of the urinary stream. Benign prostatic hypertrophy (graded 2+) was noted. Residual urine was 75 cc. He failed to return for laboratory examinations.

Seven years before his final admission, subtotal gastrectomy was done, because of gastrointestinal hemorrhage from a duodenal ulcer.

Six years before his final admission gangrene of the left foot necessitated supracondylar amputation. His diabetes was well controlled with diet and insulin (NPH, 25 units). Urinalysis showed trace albumin, occasional red blood cells and 8 to 10 white blood cells per high powered field. Specific gravity was 1.024.

Five days before his final admission he was sent to the outpatient department by his nursing home because of lethargy and refusal to eat or take medicines. Complaints at this time included increased urinary frequency (every hour while awake), nocturia (5×), hesitancy and decreased force of the urinary stream. For reasons that are not clear, the patient had been digitalized on a maintenance dose of digitoxin .2 mg. per day, by his private physician. His insulin requirement had increased to 65 units of NPH per day. No insulin had been taken for three days prior to this visit. The blood pressure was 120 mm. mercury systolic, 80 diastolic, the pulse 100, temperature 98 degrees and body weight 140 pounds. Findings included bilateral cataracts, benign prostatic hypertrophy (graded 2+), a supracondylar amputation of the left lower extremity and absent popliteal and pedal pulses in the right lower extremity.

The hemoglobin was 14.7 gm. %, white blood count 11,850, blood urea nitrogen 24 mgm. %. A fasting blood sugar was 278 mgm. %. Electrocardiogram showed a sinus tachycardia with left axis deviation, first degree heart block and depressed ST segments. The urine was acid with specific gravity 1.024, albumin 1+, sugar negative and acetone trace. The urinary sediment showed 4+ pus cells per high powered field.

The bladder was catheterized with difficulty; 300 cc. of cloudy residual urine was obtained. This urine was cultured. The patient was to return in one week for prostatic surgery.

Because of increasing lethargy and fever he was admitted three days later. The temperature was 105 degrees rectally. Respirations were 50, pulse 148 and regular and blood pressure 150 mm. mercury systolic, 50 diastolic. The right pupil was slightly larger than the left. Bilateral cataracts precluded adequate fundusoscopic examination. The neck was not rigid but some resistance to flexion was present.

A few crackling rales were audible over the base of the right lung posteriorly. The left border of cardiac dullness was percussed in the 5th intercostal space 10 cm. from the mid-sternal line. Neurologic examination was normal. No response to pain was obtained.

Bowel sounds were decreased. The dome of the bladder was palpated at the level of the umbilicus. Catheterization yielded 1,500 cc. of cloudy urine.

Continued

The hemoglobin was 13.3 gm. %, white blood count 22,100, differential count 96% neutrophils, 3% lymphocytes and 1% monocytes. Urinalysis showed specific gravity 1.019, 2+ albumin, 3+ sugar, and trace acetone. Urinary sediment was packed with white blood cells and had four red blood cells per high powered field. The blood sugar was 333 mgm. %.

The chest x-ray was normal. Blood pH was 7.42, pCO_2 was 34 mm. of mercury. The serum sodium was 136 meq./L. potassium 3.6 meq./L. chloride 99 meq./L. and CO_2 combining power 22 meq./L. The electrocardiogram was unchanged except for increased S-T segment depression.

Staphylococcus aureus had grown from the urine obtained in the outpatient department five days previously. After blood cultures were obtained, the patient was treated with penicillin (6 million units per day) and tetracycline (4 gm. per day) intravenously. Within 24 hours the temperature had decreased to 99 degrees rectally.

Staphylococcus aureus had grown from the blood on the third hospital day. Organisms from the blood and urine had identical antibiotic sensitivities. Procaine penicillin, 600,000 intramuscularly every 12 hours, and tetracycline, 500 mgm. by mouth, were substituted for the intravenous medications.

The patient became more responsive. He was able to sit up and eat. Regular insulin, 10 to 30 units per day, was used to control glycosuria. The temperature varied between 99 and 101 degrees rectally over the next four days.

On the sixth hospital day the patient became more lethargic, temperature was 103.2 rectally, pulse 140, respirations 30. Examination was otherwise unchanged. A lumbar puncture showed clear fluid. Spinal fluid pressure was 122 mm. of spinal fluid. Proteins and cells were normal.

The blood sugar was 384 mgm. %. Urinalysis showed specific gravity 1.024, trace albumin, 4+ sugar and was acid. The sediment contained 65 red blood cells and 6 white blood cells per high powered field. Blood pH was 7.41 and pCO_2 29. The serum sodium was 146 meq./L, potassium 5.6 meq./L, chloride 111 meq./L, and CO_2 combining power 17 meq./L.

The patient died the eighth hospital day.

Discussion

Dr. William Torp:*

This man's disease had progressed to the point where he had multiple diabetic complications, i.e., bilateral cataracts, renal disease and peripheral vascular involvement which necessitated amputation of his lower extremity. I would predict that retinal changes were present but could not be detected because of cataracts. One gains the impression from the protocol that we were dealing with a rather unreliable patient who failed to keep his clinic appointments and probably failed to follow instructions regarding regulation of his diabetes. Evidently diabetic control was not difficult to maintain during his previous hospitalizations. I searched for an obscure diagnosis in this patient but none was evident, and I feel that he probably died from an acute complication of his diabetic state. I should like to discuss this case in the order of the events that occurred, pointing up either their merits or the demerits.

This patient's diabetic control was probably never optimal since glycosuria was generally present on his hospital admissions. This, coupled with his failure to return to clinic, would suggest that this man took his insulin quite sporadically. The only insulin regulation that we are aware of was when he was hospitalized and was relatively easily controlled. He was not a good clinic attender. While there is some discussion about how closely a maturity onset diabetic should be controlled, the general feeling is that blood sugars should be kept as near normal as possible with the objectives of avoiding hypoglycemic episodes and controlling hyperlipemia. Patient reliability is an important factor in the adequacy of diabetic control. With many patients control is satisfactory when they are spilling a minimal amount of sugar in their urine and

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have a minimal hyperglycemia. We would rather control them in this fashion than chance a hypoglycemic reaction.

This patient's first indication that he was going to be a problem occurred fourteen years prior to his current admission when benign prostatic hypertrophy was noted. Failure to keep his clinic appointments resulted in an incomplete evaluation at that time.

Seven years prior to his admission the patient had a subtotal gastrectomy. We must assume that the diabetes was adequately controlled and that urinary tract symptoms were minimal during hospitalization. Retinal changes are not mentioned. The blood pressure is not recorded.

Six years prior to his current admission an above-the-knee amputation was necessary, and we might assume at this time that his vascular disease was becoming evident. Urinalysis now shows some renal involvement with albuminuria and red and white cells in the sediment.

This takes us to our final contact with the patient, and I think we can assume that he has widespread vascular disease at this time. We have now an ill white male who presents with two danger signs, the complaints of anorexia and lethargy. These are often the first indications we have that the patient may be acidotic, but we know that maturity onset diabetes seldom develop keto acidosis. According to the protocol the patient had had no insulin for three days prior to his being seen here. At this time he is using 65 units of NPN insulin, but we have no information about his diabetic control. He is again showing signs and symptoms of urinary outlet obstruction, and we must be overly suspicious of urinary tract infection. An estimated 20 to 40% of diabetics will develop pyelonephritis.

It is also important to note that the patient is now taking digitoxin — 0.2 milligrams per day. He is 69 years old, weighs 140 pounds and has renal impairment. I therefore think it is quite likely that this dose of digitoxin for this particular patient is much too high. According to Friedberg this is the upper limit for a maintenance dose, and it is at this level that we might well expect complications. The reasons for originally digitalizing this patient are not stated. The tachycardia and first degree heart block on the electrocardiogram, in addition to the depression of the ST segments, would add to our suspicions of digitalis intoxication. Digitalis intoxication might also cause symptoms of anorexia and lethargy. We do not know whether his digitalis was stopped, or whether he was treated for digitalis intoxication.

Laboratory investigation indicates that the patient is not acidotic. The diabetic with marked renal involvement may have a high threshold for glucose excretion in the urine, and therefore the urine sugars may not be nearly as helpful as in one who has relatively normal renal function. Urinalysis indicates a probable urinary tract infection, and again there were symptoms of probable bladder outlet obstruction. A note is made that the patient was catheterized with difficulty and a significant residual volume obtained. In an elderly patient, particularly if that patient is diabetic, one can almost predict that he is going to get into trouble with his urinary tract following such a procedure.

We do not know the exact onset of this man's difficulties, but from his continuing course one might expect a gram-negative bacteremia, and one

Continued

could easily justify starting the patient on some therapy at the time of the difficult catheterization. The antibiotics should be started after obtaining suitable urine specimens for culture. At any rate, this man was dismissed from, or sent home from, the outpatient clinic without any treatment, whereas hospitalization was indicated.

He returns three days later quite toxic and febrile. I think most of us would assume on this admission that the man had a gram-negative bacteremia. However, we are fortunate here in that the cultures obtained in the outpatient department three days previously had returned, and it is a little surprising to find that the urine grew *Staphylococcus aureus*. However, diabetics are more prone to staph infections than nondiabetics and they do not tolerate them as well. The rales heard in his chest might indicate a pneumonia, and it must be remembered that patients who present in a dehydrated state may have a relative sparsity of pulmonary findings. On re-hydration these pulmonary findings may be quite prominent. The chest x-ray may behave similarly.

I think we should also note that for the first time the patient is observed to have anisocoria. We do not know whether this is a normal finding for this patient. Difference in pupil size of approximately a millimeter may be considered normal. If the anisocoria were prominent we might wonder about some previous head trauma, particularly a subdural hematoma, which seems to occur with unusual frequency in diabetics. The clinical course is certainly compatible with such a diagnosis. This should be followed up with a lumbar puncture and skull x-rays, and should anything suspicious be noted angiography might be indicated.

With antibiotic therapy the patient appeared to improve, he was able to sit up and eat. This still does not exclude the diagnosis of subdural hematoma. These patients will not infrequently seem to be a little better before they get worse. The anisocoria might also reflect a complication of the diabetes. Third nerve neuropathies are seen in approximately 4% of the diabetic population. The anisocoria in the diabetic may also be transient, disappearing within five to six weeks.

The repeat electrocardiogram shows no change from the previous tracing. However, the digitoxin had been stopped only three days previously, and it may take longer than this before evidence of toxicity disappears, particularly in a patient with renal impairment. Again, we have no laboratory evidence of acidosis. The antibiotics used were penicillin—6,000,000 units per day and four grams of tetracycline per day. Apparently both of these were given intravenously. The dosage of penicillin for a susceptible organism in a patient with a bacteremia seems low. Diabetics in particular do not handle staphylococcal infections well. The dosage of tetracycline on the other hand is much too high, especially in a patient with renal insufficiency. The intravenous dose of tetracycline per day should be limited to less than one gram, since complications of pancreatitis, fatty liver and renal damage have been reported, particularly in patients with some degree of renal insufficiency. After criticizing the selection and dosage used for antibiotic therapy, we find that the patient gets better. The blood cultures return, showing *Staphylococcus aureus* with the same sensitivities as the organism that was cultured from the urine. A sputum culture is not reported. The infection is now treated by decreasing the amount of penicillin and

tetracycline; the penicillin being given intravenously and the tetracycline orally. Now, even after we have a documented staphylococcal bacteremia, we still are not treating the patient adequately.

This patient should be receiving massive doses of penicillin. We must, however, always bear in mind that there is about a milliequivalent of potassium per million units of penicillin and this must be considered in our electrolyte therapy — especially with renal impairment. On the sixth hospital day the patient became quite toxic. An L.P. at this time was negative. While diabetics are particularly prone to fungal infections, such as torulosis, I think we have enough disease in this patient to explain the cause of his increasing symptoms and his death.

We now note an increase in the number of red blood cells in the urinary sediment. I presume that nothing else was evident on microscopic examination although one might expect casts and white blood counts.

Summary

We have a diabetic with rather widespread vascular disease, some renal involvement, a urinary tract infection, bacteremia, perhaps a pneumonia and probable digitalis intoxication. Urine output was maintained right up to the time of death, although in the two to three days prior to death it had decreased somewhat. This decrease amounted to approximately 1800 cc. per twenty-four hours. However, the patient was still excreting between 1500 and 2000 cc. of urine per day.

We do not have follow-up chest x-rays or follow-up electrocardiograms, and I think we still have to keep the possibility of a subdural hematoma in mind. We know that the man had a staphylococcal bacteremia. We can assume that he had a staphylococcal pyelonephritis. We might suspect that he has pneumonia and also suspect that on pathologic examination he will show marked renal changes. We might also suspect that he may have renal papillary necrosis. Although the absence of oliguria is somewhat against this diagnosis, this may occur late in the course of events. In a report in the *Journal of Urology* in 1957, of the 211 cases of renal papillary necrosis reported up to 1955, 129 were in diabetic patients. An arrhythmia secondary to digitalis intoxication cannot be excluded.

Dr. A. L. Schultz:*

Why the patient with maturity onset diabetes can withstand infection and multiple types of stress without becoming acidotic is not completely understood. I think the urinary tract findings are more compatible with a pyelonephritis than with a diabetic nephropathy. The nephrosclerotic type of diabetic nephropathy may result in a nephrotic syndrome. The diabetic is particularly prone to develop urinary tract infections and also papillary necrosis. Those that develop papillary necrosis slough out their kidneys and die in a matter of days. They develop renal failure and high fevers; examination of the urinary sediment may be diagnostic. The possibility of a renal abscess that is amenable to surgery should also be considered. Further urinary tract investigation is warranted if obstructive uropathy is strongly suspected. However, there is always the danger

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Continued

of precipitating bacteremia in the man who has co-existent pyelonephritis and urinary tract manipulation.

Pathology

Dr. John Crosson:*

At autopsy the previously mentioned AK amputation of the left leg was observed. In addition the patient had adhesive pleuritis involving both lungs and also pericardial adhesions. In addition, he also had definite evidence of arteriosclerotic heart disease with the presence of an old sub-endocardial myocardial infarction. There was no evidence of an acute myocardial infarction. A bronchopneumonia was also present. Examination of the kidneys showed definite evidence of papillary necrosis, involving the

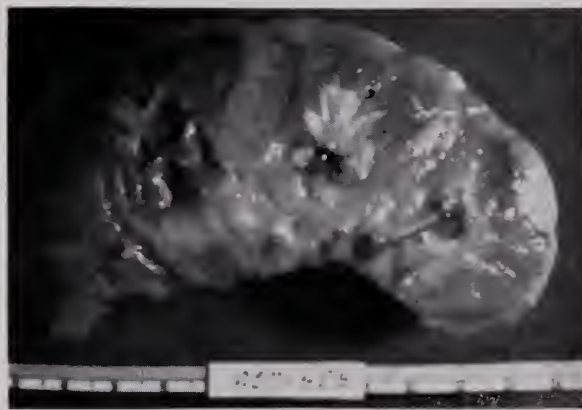


Fig. 1 — Gross picture of kidney showing papillary necrosis.



Fig 2 — Microscopic picture showing sharp demarcation between viable kidney and papillary necrosis ($\times 43$).

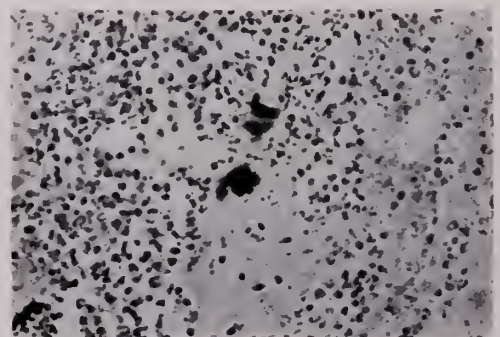


Fig. 3 — Acute pyelonephritis with clumps of bacteria in the center ($\times 43$).

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majority of the renal papillae. The necrotic papillae are sharply demarcated from the surrounding viable renal tissue. This sharp demarcation is evident both grossly and microscopically. In addition, one can see the shadows of the normal architecture maintained in the necrotic area. In association with the papillary necrosis this man had an extensive, acute pyelonephritis. Several clumps of bacteria are noted in the region of the inflammatory reaction. There was no evidence of diabetic glomerulosclerosis. Extensive arteriolar vascular disease is demonstrated by the hyalinization of the arterioles. Microscopic splenic infarcts were also present. In addition, the pancreas showed islet cell hyalinization. This man was a prime candidate for papillary necrosis. Besides being a diabetic, he also had an acute urinary tract infection with a relatively unusual organism, *Staphylococcus aureus*. In patients who develop papillary necrosis, however, this is a relatively common organism. Associated pyelonephritis is seen in practically 100% of patients with papillary necrosis.

I should like to discuss the clinical situations which should lead one to suspect papillary necrosis. In diabetics who show evidence of sepsis and urinary tract infection, this condition should be considered. Diabetics with the rapid onset of coma and a rapidly rising BUN might also have papillary necrosis.

The third large group encompasses diabetics with low-grade pyelonephritis who become acutely worse with the rapid onset of coma and deterioration. A fourth group, although relatively rare, is quite interesting. These are the people with renal colic secondary to the sloughed papillae. This presumably is also the reason for the hematuria that is frequently seen. Finally, patients with diabetic acidosis, whose acidosis is corrected chemically, but who still do not wake up, should be suspected of having papillary necrosis. As far as I know, tetracycline has not been associated with papillary necrosis.

William Torp, M.D.*
Hennepin County General Hospital

*Resident Internal Medicine.

Frontier Doctors' Self-Service

When illness struck the doctor, he was usually hundreds of miles from medical assistance and had to cure himself. Dr. M. F. Honan was a Bellevue graduate who practiced in La Grande, Oregon. One day he suffered terrible abdominal pains, diagnosed his condition as appendicitis, and operated on himself. He died under his own knife. He learned too late that he suffered not from appendicitis, but from an infected gall bladder with gallstones. Dr. George W. Mason of Klamath Falls, Oregon, proved more successful at self-surgery. As he was riding back to town on the California Road after tending to an injured freighter, his buggy wheel dropped into a muddy rut. The doctor was thrown from the seat so that his leg caught in the spokes of the wheel. The frightened horses bolted, and the doctor's leg was almost twisted off above the knee before he could bring the team to a halt. Knowing that only an immediate amputation could save his life, he cut off his limb and bandaged the stump with a silk muffler.

— Richard Dunlop, M.D.: Doctors of the American Frontier

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Diagnostics

The Diagnosis of Multiple Sclerosis*

IT IS NOT unusual in a neurological clinic to see three patients in succession with histories such as these. A lady of sixty-three years may be referred with the history that six months earlier she had suddenly developed a "numbness," a "tingling, itchy" feeling of her right antero-lateral thigh. At the onset she had consulted her physician who listened carefully and then mentioned several diagnostic possibilities, among them "something like multiple sclerosis." Over the next six months the complaint continued without change, but the lady became irritable, insomniac, anorexic and quite convinced that she was "dying of multiple sclerosis." The fact that she had a traumatic neuritis of the lateral femoral nerve (meralgia paraesthetica), a perfectly benign process, was "life saving" to her, but it did little to alleviate the six months of unnecessary anxiety.

The second patient may be a forty-two-year-old minister who awakened seven days earlier unable to close his left eye or move the left side of his face. The day after his facial trouble he became very unsteady, suffered vertigo and nausea and was unable to do his usual work. His physician was consulted at his office and both "multiple sclerosis" and "stroke" were mentioned in the differential diagnosis with less than a quieting effect on the patient. The diagnosis of geniculated herpes (Ramsey Hunt) was the accurate one and had a much less malignant connotation to the patient. He also was fortunate enough to have had a complete recovery of the facial paralysis during the following ten days.

The third patient may be an eighteen-year-old college freshman who described her trouble as being an "odd sensation of the left side of her body." The difficulty had developed over the Christmas holidays of her senior year in high school and had lasted for about three weeks. During the same period she had difficulty reading; the print of a book would "look double", especially when she was tired. Both complaints had disappeared shortly after she returned to school. In May, during preparation for the final examinations for her freshman college year, she again noticed that her left side was "different", "didn't want to work just right" and "felt numb." She consulted her physician and was told it was her "nerves" and that it would "probably be better after the examinations." This young lady showed dysconjugated movements of her eyes, a mild left sided incoordination and bilaterally positive toe signs. She had multiple sclerosis.

These three patients were a common clinical experience. The errors in the "making" and "not making" of the diagnosis of multiple sclerosis are the most numerous made in neurology. Much of the difficulty arises from the fact that since it has long been taught that the variability of this disease is quite unlimited, it is included in the differential diagnosis for any pathological involvement of the central nervous system. The difficulty is compounded by the wide-spread and

*Presented at the Black Hills Medical Seminar, August 5, 1966.

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morbid lay publicity given multiple sclerosis in an effort to raise charity donations. The disease has a malignant connotation to the patient if he is erroneously told that he "has" or "might have" difficulty.

The diagnosis of multiple sclerosis can be very subtle and difficult, but usually it is not. The vast majority of cases behave much the same, and a few general rules can assure accurate diagnosis of at least seventy-five percent. It must be remembered that this is a disorder quite peculiar to the young, the initial lesion of the nervous system commonly occurs before the thirty-fifth year. A neurological lesion which presents in old age, with absolutely no previous central nerve system difficulty is not multiple sclerosis. The lesions of this disorder occur rather acutely over days, weeks or months, but once developed they do not remain constant in the early phase. The lesions improve and the symptom-sign complex of the patient remisses or becomes markedly better. This disease never produces only one lesion for long; a neurological examination always shows more than one site of pathological change. The sites that usually are involved produce dysfunction in the corticospinal system with variations of spastic paresis, the cerebellar system with incoordination, the cranial nerves with scotomas, oculomotor dysfunction and vertigo in the sensory system, especially the dorsal columns. These general rules must be adhered to, and unless a patient satisfies all three criteria: (1) onset before the age of thirty-five years, (2) a definite course of remission and exacerbations, and (3) more than one focus of pathology within the central nervous system, a diagnosis of multiple sclerosis should not be made and should certainly not be suggested to the patient.

Further certainty in establishing an accurate diagnosis of multiple sclerosis can be assured by being aware of symptoms which it seldom or never manifests. This disorder never starts after the age of forty-five, and it never involves only one site, as its name indicates. The lesion never continues to progress slowly; it invariably improves, with some degree of remission. The disease does not produce increased intracranial pressure or papilledema, nor does it produce paroxysmal phenomena of a seizure or convulsive type. The demyelinating lesions are central and do not produce a mononeuritis. If your patient shows these symptoms multiple sclerosis is not the correct diagnosis of his malady.

These few simple rules would have avoided the errors made in each of the three cases cited; likewise, they are good rules to follow in the diagnosis of central nervous system involvement.

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St. Luke's Hospital Seminar

St. Luke's Hospital, St. Paul, is presenting a seminar entitled "Clinical Aspects of Hematology" on April 27, 1967, starting at 1:30 p.m., in the St. Luke's Hospital auditorium. The featured speaker will be Dr. A. J. Quick of Marquette University Medical School. Contact: C. E. Turbak, M.D. at St. Luke's Hospital.

Bacteremia Due to Gram-Negative Bacilli

Some Current Concepts of Therapy. Part I.*

FINLAND AND his associates,¹ McCabe and Jackson,² and members of our group³⁻⁶ have described the rate of bacteremia due to gram-negative bacilli as increasing threefold to fivefold in recent years. This presentation attempts to review the subject, with emphasis on some current concepts of its management. Such specific diseases as brucellosis, tularemia, and typhoid fever are not considered herein.

Causative Microorganisms

Only those cases in which two or more positive blood cultures were obtained and in which clinical examination showed true bacteremia have been included in our investigations.³⁻⁶ In our experience, *Escherichia coli* cause about one half of these infections; *E. coli* and *Klebsiella-Aerobacter* organisms, together, are causative in two thirds. Recently, *Pseudomonas* has displaced *Proteus* as the third most common pathogen. *Proteus* organisms cause bacteremia about twice as often as *Bacteroides*. Less common pathogens include *Paracolobactrum*, *Achromobacter*, *Salmonella*, *Shigella*, and *Alcaligenes*.

Pseudomonas organisms, although normal bowel inhabitants, are widely distributed in nature and are found in water, on skin surfaces, and in the air, giving them access to wounds, drugs, and medical instruments. Ordinarily, *Pseudomonas* organisms have little talent for sustained invasion, but when host defenses are incompletely developed, as in infants, or when defenses are weakened, as in debilitated adults, they can cause serious infections. The frequency of *Pseudomonas* infections may partly reflect the organisms' resistance to most antimicrobial

agents, allowing their emergence as predominating microbes when other bacteria are eradicated. Also, aging of the population, prolongation of life in patients with weakened defenses, and predisposing medical procedures may be contributing factors.

Bacteroides are anaerobic bacilli inhabiting such areas as the nasopharynx, bowel, and female genital tract. To detect *Bacteroides* bacteremia, all blood drawn for cultures should be inoculated into anaerobic media, such as deep tubes of dextrose brain broth. In about one third of patients having *Bacteroides* bacteremia, the bacilli are identified within 48 hours after inoculation of cultures, but in two thirds, incubation times range from 5 to 20 days. In about one fifth of patients having *Bacteroides* bacteremia, additional organisms, usually streptococci, are isolated simultaneously.

Age and Sex of Patients

In our experience, twice as many men as women have bacteremia of this type. More than 75% of the men are 50 years old or older; about 40% of the women are less than 50 years. Only about 10% of our patients have been less than 30 years old; susceptible persons of this age include (1) women in the postpartum state or undergoing septic abortion, (2) children with severe burns, malignant neoplasms, or hematologic diseases, and (3) premature infants.

Portal of Entry

In about 50% of our cases there was a urinary portal of entry. The biliary tract was the portal in 10%, and the rest of the gastrointestinal tract in 15%. The female genital tract was indicted in 5%. In another 5%, other sources such as skin, postopera-

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*Read at the meeting of the American Academy of General Practice, Lake Okoboji, Iowa, June 18, 1966.

tive wounds, and the respiratory tract were responsible. In 15% of our cases a portal was not evident. In 50% this type of bacteremia has occurred after surgical or manipulative procedures; two thirds of the procedures were genitourinary and one third, gastrointestinal.

The respiratory tract, although not a common portal for gram-negative bacteremia in general, may give entry to *Bacteroides* infection. *Pseudomonas* bacteremia also has had a respiratory portal, as in patients inhaling contaminated aerosols; but such portals as the skin in victims of burns and the urinary tract are more common in *Pseudomonas* infection. These portals for *Pseudomonas* bacteremia share the possibility of exposure to contaminated instruments and medications.

In the 15% of our cases in which a portal was undetected, there was a high incidence of hematologic disease. Hematologic disease, contradistinct to other predisposing conditions, is usually characterized by a clinically inapparent portal for supervening bacteremia. Recent studies in fatal cases of bacteremia due to gram-negative bacilli disclosed that nidi of infection in the lung and mucous membranes of the upper respiratory passages and alimentary tract were the sources of bacteremia in most patients with hematologic disease.⁷

Predisposing Nidi of Infection

Among nidi of infection from which bacteremia may originate, in our experience pyelonephritis, cholangitis, and conditions associated with varying degrees of peritonitis, such as appendicitis and diverticulitis coli, are most common. Cutaneous, respiratory, and other nidi of infection are less common. These nidi are often disturbed by surgical or manipulative procedures or are associated with other predisposing disease or treatment that alters host mechanisms involved in localizing infection.

Predisposing Noninfectious Diseases

Advanced arteriosclerosis, which occurred in about 20% of our patients, may be indirectly predisposing because victims of

strokes, and those undergoing surgery for abdominal aneurysms and the like, frequently require urinary catheters. Infected peripheral gangrene is an additional and more direct portal.

Malignant neoplasms were present in about 10% of our patients; in three fourths of these, bacteremia occurred after urologic procedures or gastrointestinal operations. Bacteremia also followed certain medical regimens, especially the use of radiomimetic drugs.

Hematologic disorders were present in about 15% of our patients. Diminished resistance to infection in these diseases may reflect (1) defects in gamma-globulin, as in chronic lymphatic leukemia, lymphoma, and multiple myeloma; (2) inadequate neutrophilic response, as in acute leukemia, chronic granulocytic leukemia, agranulocytosis, or aplasia; and (3) iatrogenic factors including therapy with adrenal steroids, antimetabolites, and antibiotics. In hematologic diseases, bacteremia is not uncommonly due to *Pseudomonas* organisms, to bacteria infrequently causative otherwise of overwhelming infection such as *Alcaligenes* organisms; and the incidence of polymicrobial infection is higher also.⁸

Of our patients, about 10% had diabetes mellitus in which the portal is almost always urinary.⁹ Diabetic complications like coma, cesarean section, and amputation frequently require urinary catheterization, further enhancing bacteremia.

Five per cent of our patients had severe hepatic disease in which bacteremia may reflect "reseeding" of the blood with bacilli phagocytized, but not killed, in Kupfer's cells. In such patients the number and phagocytic activity of Kupfer's cells are normal, but the cells appear unable to destroy ensnared organisms. In our experience, infectious nidi in the biliary passages, urinary tract, or peritoneum, especially if disturbed by surgery or manipulation, appear to be the sources of bacteremia in most of these patients.¹⁰

Predisposing Therapies

Predisposing therapies include surgery and instrumentation, as occurred in about

half our cases. Two thirds of these procedures were genitourinary and one third were gastrointestinal. The most common procedure was transurethral prostatic resection, with cystoscopy a close second. Among gastrointestinal procedures, the three most common operative sites were the biliary tract, the intestines, and the stomach. Bacteremia, especially that due to *Pseudomonas* organisms, may occur on contamination of a heart-lung machine or hemodialysis apparatus; fortunately, in our group practice, bacteremia has not occurred after infusion or transfusion.

In about 20% of our patients, the penicillins and allied drugs administered prior to the onset of bacteremia appeared to have depressed gram-positive elements of the normal microflora, allowing overgrowth and bloodstream invasion by gram-negative elements.

In 15% of our cases adrenal glucocorticoids had been employed before the onset of bacteremia, most often to control hematologic diseases. McCabe and Jackson² noted that prior administration of steroids increased the frequency of bacteremic shock and the fatality rate among their patients.

Five per cent of our patients were receiving antimetabolites when bacteremia occurred; these patients had hematologic or malignant disease.

Less than 5% of our patients were receiving irradiation when bacteremia occurred; these patients also had hematologic or malignant disease.

Other potentially predisposing therapies include the subcutaneous or intramuscular injection of contaminated medications, the inhalation of contaminated aerosols, and "cut-down" sites and areas of thermal trauma which become infected.

Clinical Features

About 98% of our patients had fever that ranged from 101 to 106 F (oral); such fever may be intermittent, remittent, continuous, or variable. The onset of bacteremia is manifested by fever and chills in about 60% of patients, by spiking fever without chills in approximately 25%, and by a gradual onset of malaise and fever in about

15%. Twenty to 30% manifest their infection by sudden circulatory collapse, or bacteremic shock.

Headache is common. All patients have some degree of prostration, but delirium and stupor are rare. Vague myalgia, restlessness, apprehension, and agitation are initial manifestations in a few patients. Coma is rare and usually reflects an underlying condition, such as hepatic failure, uremia, or diabetic acidosis. Anorexia is usual, but vomiting, abdominal distention, and diarrhea often reflect an underlying disease such as chronic ulcerative colitis, uremic enterocolitis, or pelvic abscess. Diarrhea can be manifest in bacteremia in the absence of underlying intestinal disease, and classically this suggests *Bacteroides*¹¹ or *Salmonella* infection, although it may also be associated with infection due to other gram-negative bacilli. Diarrhea occurring after bacteremia is established should suggest staphylococcal enterocolitis complicating antibiotic therapy. Hyperventilation in our experience is more characteristic of advanced shock and has not been a common presenting sign of that complication.

Leukocytosis is usually present, but a normal number of leukocytes is not rare. In an occasional case, leukopenia shortly replaced by leukocytosis is the initial manifestation of complicating shock. In some cases of established *Pseudomonas* bacteremia, marked and persistent leukopenia occurs. Mild anemia is common. Of course, these generalizations may be considerably modified by findings in patients having underlying hematologic diseases.

Albuminuria, hematuria, and pyuria usually reflect underlying disease. Azotemia, hyperkalemia, and decreased values for serum sodium, chloride, and carbon dioxide-combining power occur especially in patients having an hypotensive episode. Recently, the concentrations of lactate and pyruvate in the blood have been studied as possible indices of impending shock and its reversibility. Metabolic acidosis, which is common in bacteremic shock, may be due largely to an increase in lactate radicals.¹² As a pre-

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liminary impression, the severity of shock appears to parallel the concentration of blood lactate; a high level of blood lactate, or lacticacidosis as it has been called, early in shock appears to indicate a poor prognosis. An initial value of less than 10 mEq per liter which drops rapidly with treatment may indicate a better prognosis. Significant lacticacidosis occurs when the ratio of lactate to pyruvate is greater than 10 to 1. The correlation appears to be good between rising levels of blood lactate and decreasing values for serum bicarbonate and arterial pH. The genesis of lacticacidosis appears to reflect tissue hypoxia resulting from reduced blood flow which increases anaerobic metabolism with a consequent rise in lactate levels. An elevated value for serum phosphate in the presence of acidosis may indicate lacticacidosis. A corroborative test of significant lacticacidosis is the determination of the anion gap $[(Na + K) - (HCO_3 + Cl)] = 17$ mEq/L wherein a gap greater than 17 is taken as being representative of true acidosis. Removal of lactic acid from the blood appears to be a function of the liver and consequently lacticacidemia may occur when the blood supply of the liver is impaired or the liver is damaged by disease. In such patients as those having impaired renal function or diabetes mellitus, one should not fail to consider the multiple factors possible in the genesis of the acidosis.

Notable clinical features sometimes suggest that the pathogen is *Pseudomonas*. First are skin lesions, most often seen in the anogenital regions and axillae and known as "ecythma gangrenosum." The lesions begin as macules or vesicles, become pustular, and may slough to form necrotic ulcers. Biopsy of the lesions may reveal bacilli in the walls of blood vessels, and culture may reveal the *Pseudomonas* organisms. Another possible feature of *Pseudomonas* bacteremia is severe leukopenia, at times associated with thrombocytopenia. One notes that patients with underlying hematologic disease are predisposed to *Pseudomonas* bacteremia. Conversely, in those without such underlying disease in whom *Pseudomonas* bacteremia develops, secondary

hematologic findings may be a manifestation of the infection. Petechiae and rarely bluish green discoloration of the nail beds also may characterize *Pseudomonas* bacteremia. Jaundice may be noted in bacteremia due to other gram-negative bacilli but is of increased incidence in *Pseudomonas* bacteremia.

Diarrhea beginning prior to antibiotic therapy and ceasing with recovery occurs in about one third of cases of *Bacteroides* bacteremia. Diarrhea suggests *Bacteroides* or *Salmonella* infection but also is noted in bacteremia due to other gram-negative bacilli. In about one third of cases of *Bacteroides* bacteremia, foul-smelling exudates are noted, but only rarely do these have the stale, butterlike, or cheesy odor said to be characteristic of *Bacteroides* infection. Delayed response in *Bacteroides* bacteremia suggests the likelihood of a suppurative locus, requiring surgical drainage. However, control of *Bacteroides* bacteremia, even in the absence of localized suppuration, may require more time than does bacteremia due to other gram-negative bacilli. Localized suppuration occurs in bacteremia due to other gram-negative bacilli but appears to be of higher incidence in *Bacteroides* bacteremia. Unlike the findings of other investigators, clinical evidence of thrombophlebitis has not been common in our patients with *Bacteroides* bacteremia.¹¹

When bacteremia complicates septic abortion, one considers coccal and clostridial infection, but gram-negative bacilli commonly are responsible; smears of the cervix may aid in this distinction prior to reports of blood cultures.

Complications

Bacteremic shock due to gram-negative bacilli is said to be present when the following criteria are fulfilled: (1) a sustained, often precipitous, drop in systolic blood pressure to 80 mm. of mercury or below is noted in an individual previously normotensive; (2) gram-negative bacilli are recovered from blood cultures obtained during or shortly preceding the hypotension; and (3) the clinical picture is compatible with bacteremia, with other causes of shock excluded.

The blood pressure may not faithfully reflect the status of the microcirculation to various organs; consequently, inadequate tissue perfusion may be present prior to development of hypotension. Nevertheless, sustained systemic arterial hypotension remains an essential clinical manifestation of bacteremic shock since more sensitive methods of detection are presently unavailable.

The precise pathogenesis of human bacteremic shock is at best incompletely understood. Normal blood pressure reflects a satisfactory relation of vascular capacity to blood volume; significant change in either of these variables is reflected by a change in the blood pressure. When vascular capacity is increased by dilatation of the vessels, blood is sequestered therein and diminished amounts are returned to the heart. Incomplete cardiac filling results in reduced cardiac output, hypotension, and diminished arterial blood flow. Consequently, there is inadequate perfusion of vital tissues and organs with oxygenated blood. Although definite proof is lacking, liberation of the endotoxin of gram-negative bacilli into the systemic circulation likely initiates the complex pathophysiologic response present in bacteremic shock. Microcirculatory experiments indicate that endotoxin acts indirectly on blood vessels, apparently through the medium of a heat-labile component in blood, and induces tetany-like activity of the vascular bed near the arteriolar level. Initially vasoconstriction predominates, but eventually there is vascular atony with consequent stagnation of blood in the peripheral capillary beds. The resulting decreased cardiac filling may eventuate in diminished arterial blood flow as previously noted, the consequence being that anoxia prevents normal cellular metabolism and that anaerobic cellular reactions dominate, with formation of acid metabolites to the point of metabolic acidosis. It should be stressed that in bacteremic shock, blood volume usually is adequate but perfusion is ineffective because of peripheral pooling. As data accumulate, it becomes apparent that human bacteremic shock is not the result of a single hemodynamic aberration;

some patients have reduced cardiac output and normal or increased peripheral arterial resistance, whereas others may have essentially normal cardiac output and reduced peripheral arterial resistance.

In these cases, shock may be obscured by warm skin, bounding pulse, and fever, and only hypotension may indicate the presence of shock clinically. The synoptic symptomatology of bacteremic shock consists of increasing temperature and pulse rate, with decreasing blood pressure and urinary output. As a generalization, in patients having advanced bacteremic shock, frequently there is a reduction in urine flow to 20 ml. or less per hour. The complication has two symptomatic and prognostic stages. In stage I, which is characterized by "infectious" symptomatology, the patient is alert and has warm flushed skin, full bounding pulse, progressive pyrexia, moderate hypotension, and moderate urinary output. If the complication is recognized in stage I and appropriate treatment instituted, the prognosis is good. In stage II, which is characterized by "shock" symptomatology, the patient is semicomatose and has pallid, cold damp skin, collapsed superficial veins, feeble pulse, shallow hyperpnea, marked hypotension, and progressive oliguria, and the prognosis is poor.

In addition to bacteremic shock, there are two other significant complications of bacteremia due to gram-negative bacilli and its management, namely metastatic suppuration and superinfection. *Bacteroides* organisms, although not the sole bacterial cause of metastatic infections, have an increased propensity to cause such lesions. Metastatic infections may include abscesses of the liver, lung, and kidney.

In 5 to 10% of cases, superinfections occur; these include enterocolitis, bacteremia, pneumonia, pyelonephritis, and parotitis. Staphylococci usually are responsible, but sometimes other organisms, such as *Streptococcus faecalis* are causative. Approximately one fourth of superinfections are fatal; but malignancy, leukemia, and the like usually cause the death.

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Antibacterial Therapy

In-vitro inhibition tests are mainly of retrospective value in the management of bacteremia, because therapy often is begun empirically before such data are available. To postpone therapy until the results of such tests are reported would mean a delay of 24 to 48 hours and an increased chance of mortality. Awareness of a primary nidus of infection, underlying disease, or predisposing therapy may suggest causation by gram-negative bacilli and initiation of a pertinent regimen until microbiologic data are forthcoming.

My colleagues and I initiate empiric antibiotic therapy, either on report of positive blood cultures or in cases wherein bacteremia is likely, when blood has been drawn for culture. In our cases, a tetracycline and streptomycin, or alternatively, chloramphenicol and kanamycin, have been the regimens given most often under these circumstances.

If on subsequent receipt of inhibition tests the bacilli resist the drugs being given and if the patient is not progressing well, the empiric regimen is changed. In cases wherein progress has been unsatisfactory after 12 to 24 hours and inhibition tests remain unreported, the regimen may be changed empirically. In the latter cases, in addition to the two regimens mentioned, one considers use of polymyxin B or colistin in replacement of streptomycin or kanamycin. More recently we have been investigating the combined use of cephalothin and colistin (or polymyxin B) given under these circumstances. Other possible empiric regimens that may warrant investigation are cephalothin plus kanamycin and ampicillin given with kanamycin, colistin and polymyxin B.

In actual management of these patients, on report of positive blood cultures or after blood is drawn for culture in those having clinical bacteremia, 500 mg. of a tetracycline or chloramphenicol is given by mouth every six hours. If shock jeopardizes intestinal absorption, a tetracycline is given intravenously in amounts of 500 mg. every eight to 12 hours. Alternatively, chloramphenicol can be given intravenously in similar amounts every six to eight hours. As much

as 1 gm. of streptomycin — or 0.5 gm. of kanamycin if associated staphylococcal infection or refractoriness appears to indicate — is given intramuscularly every 12 hours. When polymyxin B or colistin is used, 50 mg. is given intramuscularly every 6 to 8 hours. Cephalothin is given in amounts of 0.5 gm. every four to six hours intramuscularly, or 1 gm. may be given at the same time intervals, or more often by the intravenous route.

If renal function is impaired, the dose of the tetracycline, streptomycin, kanamycin, polymyxin B, or colistin is correspondingly reduced.

There are disadvantages of empiric use of combined antibiotic therapy. These include the dual depressive effect on the gram-negative elements of the flora, making superinfection more likely. However, periodic study of the sputum and stools during therapy may reveal any floral changes and impending superinfection. Streptomycin, kanamycin, polymyxin B, colistin, and possibly cephalothin are nephrotoxic; excepting cephalothin, these drugs may cause a curariform effect that is manifested by respiratory depression. Chloramphenicol is hematotoxic. Streptomycin and kanamycin are ototoxic, but the latter is more likely to cause deafness. Polymyxin B and colistin also may cause cerebellar ataxia and other neurologic complications. In view of current results on in-vitro tests of bacterial susceptibility, which will be discussed in greater detail later, streptomycin-tetracycline may not provide antibacterial "coverage" to the degree obtainable with alternative regimens. Moreover, combined therapy entails the introduction, or an increased number, of parenteral injections and is more expensive.

It may be pertinent to recall that the incidence of ototoxicity after use of streptomycin is minimized if one avoids a dose in excess of the patient's renal tolerance and administers it for a minimal period. Fear of ototoxicity should not completely interdict use of streptomycin, but one should not give it indiscriminately. Perhaps one should exercise greater caution in the use of kanamycin, since it is more likely to cause deafness and,

like dihydrostreptomycin, has caused deafness of delayed onset. Streptomycin is more likely to cause vestibular damage, which can be compensated considerably by visual mechanisms.

With the advent of newer drugs, we have reevaluated our policy of the empiric use of combined antibiotic therapy. Use of colistin as a single agent, like polymyxin B, has a disadvantage because *Proteus* and *Bacteroides* organisms usually are resistant to it. Kanamycin is inadequate, as a single agent, because a number of *Pseudomonas* and most *Bacteroides* are insensitive. Ampicillin is inactive against most *Klebsiella-Aerobacter* organisms, most *Proteus* bacilli that are indole-positive, and *Pseudomonas* organisms. Cephalothin is not active against all *Klebsiella-Aerobacter* organisms, *Bacteroides*, and indole-positive *Proteus* bacilli and usually is inactive against *Pseudomonas*. To date, there is no single agent available that assures complete "coverage" against gram-negative bacillary infections. As aforementioned, we are currently investigating cephalothin and colistin (or polymyxin B) given in combination in the empiric management of bacteremia due to gram-negative bacilli. Possible a priori objections to this combination are that all indole-producing *Proteus* organisms and *Bacteroides* may not be susceptible to its effect; however, thus far the regimen has been very satisfactory.

Exemptions from the empiric rule of combined antibiotic therapy depend on various features in the individual case, examples of which include (1) identification of the pathogen, that is, identification of *Pseudomonas* would indicate use of polymyxin B or colistin, (2) refractoriness to the empiric regimen, or (3) the reporting of tests of in-vitro bacterial susceptibility indicating a single agent to be effective.

Currently, when the patient's course is unsatisfactory and microbiologic data are reported, the empiric regimen may be replaced with a more pertinent drug, in keeping with results of tests of in-vitro bacterial susceptibility. Against *E. coli*, such drugs as ampicillin, cephalothin, polymyxin B, or colistin

may be applicable. However, some workers avoid the use of polymyxin B and colistin when possible in nonpseudomonal infections because the drugs may produce relatively low serum and tissue levels. As a generalization, strains of *E. coli* are susceptible to streptomycin and the tetracyclines and cephalothin in about 50% of cases; these bacilli are susceptible to kanamycin, chloramphenicol, and ampicillin in 80% or more of cases. The same generalization is applicable to *Klebsiella-Aerobacter* organisms except that only about 10% of these bacilli are susceptible to ampicillin.

Among other drugs, penicillin G, ampicillin, cephalothin, and novobiocin are active against the indole-negative *Proteus mirabilis*, which causes 80 to 90% of clinical infections due to *Proteus* organisms. Cephalothin is active in 10 to 20% of infections caused by indole-positive *Proteus* organisms, that is, *P. vulgaris*, *P. morganii*, and *P. rettgeri*; chloramphenicol also may be effective, but differences between in-vitro and in-vivo results are frequent with the drug against these organisms. Consequently, kanamycin may be the drug of choice against indole-positive organisms. Polymyxin B or colistin is used especially against *Pseudomonas* organisms. Despite the availability of the newer agents, a tetracycline often is preferred in bacteremia due to *Bacteroides* organisms; penicillin G may be active against certain strains of *Bacteroides*. Ampicillin, cephalothin, and kanamycin, in addition to the tetracyclines and chloramphenicol, may be applicable to *Salmonella* infections. It is to be noted that cephalothin may not eradicate infections due to certain gram-negative bacilli, including *Salmonella*, despite in-vitro indications of susceptibility.

The use of intravenously administered penicillin G in doses of 20,000,000 to 60,000,000 units daily has been suggested in infections due to *Enterobacteriaceae*, excepting *Proteus* organisms. *P. mirabilis* is sensitive to smaller dosage, whereas other *Proteus* organisms are resistant to even heroic doses. Because other effective drugs have become available, currently there is infrequent need

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of penicillin G therapy for infections due to *Enterobacteriaceae*, except for some of those due to *P. mirabilis*.

It may be pertinent to mention here that strains of bacteria may resist antimicrobial drugs because these organisms carry so-called R (resistance) factors. The R factor appears to represent genetic material (DNA) not attached to the bacterial chromosome but floating free in the bacterial cytoplasm. This extrachromosomal material appears to be transferable among organisms by bacterial conjugation; antibiotic-resistant bacteria can transmit the property of resistance to susceptible bacteria when grown together. Transfer of resistance has been noted among the *Enterobacteriaceae* as well as among *Pseudomonas* organisms and staphylococci. The incidence of bacterial strains carrying R factors appears to have increased in direct proportion to the use of antibacterial agents.

Clinical circumstances were such that a single agent has been employable in little more than one third of our cases. There is no argument against the premise that best results are obtained when the bacilli are susceptible in vitro to the drug employed, but the difficulty lies in the unavailability of such data when the clinical status of the patient requires initiation of therapy.

Since polymicrobial infections are of increased incidence in *Bacteroides* bacteremia and in patients with hematologic diseases, several drugs may be given simultaneously: for example, tetracycline for *Bacteroides* and penicillin G and streptomycin for an enterococcus. However, one tries to minimize the number of drugs because their indiscriminate uses may increase bacterial resistance, since such resistance appears to manifest the amount of a drug used in a given area. Ampicillin and cephalothin may prove useful in selected polymicrobial infections.

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References

1. Finland, M., Jones, W. F., Jr., and Barnes, Mildred W.: Occurrence of Serious Bacterial Infections Since Introduction of Antibacterial Agents. *JAMA* 170:2188, 1959.
2. McCabe, W. R., and Jackson, G. G.: Gram-Negative Bacteremia. I. Etiology and Ecology. *Arch Intern Med (Chicago)* 110:847, 1962.
3. Martin, W. J., and McHenry, M. C.: Bacteremia due to Gram-Negative Bacilli: Résumé of Experiences in 303 Cases. *J Lancet* 84:385, 1964.
4. McHenry, M. C., Martin, W. J., and Wellman, W. E.: Bacteremia due to Gram-Negative Bacilli: Review of 113 Cases Encountered in the Five-Year Period 1955 Through 1959. *Ann Intern Med* 56:207, 1962.
5. Spittell, J. A., Jr., Martin, W. J., and Nichols, D. R.: Bacteremia Owing to Gram-Negative Bacilli: Experiences in the Treatment of 137 Patients in a 15-Year Period. *Ann Intern Med* 44:302, 1956.
6. Martin, W. J., and McHenry, M. C.: Fifty-nine Cases of Bacteremic Shock due to Gram-Negative Enteric Bacilli. *Med Clin N Amer* 46:1073, 1962.
7. McHenry, M. C., Baggenstoss, A. H., and Martin, W. J.: Bacteremia due to Gram-Negative Bacilli: Clinical and Autopsy Findings in 33 Cases. (Submitted for publication.)
8. McHenry, M. C., Martin, W. J., Hargraves, M. M., and Baggenstoss, A. H.: Bacteremia in Patients With Neoplastic or Hematologic Disease. *Mayo Clin Proc* 37:43, 1962.
9. Martin, W. J., and McHenry, M. C.: Diabetes Mellitus Complicated by Bacteremia Caused by Gram-Negative Bacilli: Further Observations. *Mayo Clin Proc* 36:507, 1961.
10. Martin, W. J., McHenry, M. C., Wellman, W. E., and Baggenstoss, A. H.: Severe Liver Disease Complicated by Bacteremia: Further Observations on Gram-Negative Bacilli. *Arch Intern Med (Chicago)* 109:555, 1962.
11. McHenry, M. C., Wellman, W. E., and Martin, W. J.: Bacteremia due to *Bacteroides*: Review of 11 Cases. *Arch Intern Med (Chicago)* 107:572, 1961.
12. Peretz, D. I., McGregor, M., and Dossetor, J. B.: Lacticacidosis: A Clinically Significant Aspect of Shock. *Canad Med Ass J* 90:673, 1964.

The Patient's Right and Duty

*One who is ill has not only the right but also the duty to seek medical aid. —
Maimonides (1135-1208)*



Grand Rounds

*Pseudomembranous Enterocolitis**

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Medical Resident

PSEUDOMEMBRANOUS ENTEROCOLITIS is a disease of obscure etiology. Although awareness of the entity goes back to the 1800s, much remains unanswered as to etiology, pathogenesis, and therapy. Controversy persists regarding the relationship to staphylococcal enterocolitis. Synonyms that are commonly found in the literature include diphtheritic colitis or enterocolitis, acute necrotizing hemorrhagic enterocolitis, staphylococcal enterocolitis, and ischemic colitis.

History

Birnbaum¹ refers to a description of this entity by Billroth in 1867 in which the possibility of sepsis producing the lesion was mentioned. However, Finney is credited with the first published account of this process.² In 1893 he described a case of bloody diarrhea that occurred 10 days after gastric surgery in a 22-year-old negro female. The patient died eight days later and at autopsy showed "diphtheritic" enteritis of the terminal ileum and colon. No enteric pathogens were found and the microscopic sections were not described. However, Bennett et al. reviewed the sections in 1956 and noted numerous gram-positive cocci in the intestinal wall.²

Scattered reports³ early in the 20th century include Riedel's description in 1902 of five postoperative patients who developed a clinical picture of diarrhea and circulatory collapse and died within four or five days from the onset of symptoms. At autopsy "diphtheritic" lesions of the intestine were found. In 1910 Wertheim described "diphtheritic" enteritis in three patients in a series of 500 cases of radical pelvic exenteresis for carcinoma of the cervix.

The first large series analyzed in this country was that of Penner and Bernheim⁴ in 1939, consisting of a review of 40 cases over a 10-year

*Medical Grand Rounds, Hennepin County General Hospital, June 21, 1966.

Continued

period. They discussed the occurrence of the lesion subsequent to such operative procedures as craniotomy, radical mastectomy, and lobectomy, as well as abdominal surgery. They also discussed its occurrence in such nonsurgical disorders as extensive burns, gastrointestinal hemorrhage, and fractures of the spinal column without operation. It was suggested that shock was the common denominator associated with the disease, and it was proposed that this was of etiologic significance.

Dixon and Weisman⁵ reviewed records at the Mayo Clinic for a 10-year period and added 23 cases to published accounts of the occurrence of the entity in postoperative patients. In their series circulatory collapse was associated with the clinical onset of intestinal complications. It was observed that the interval between shock and death was so brief in many cases that it was unlikely that the pseudomembranous lesions could have developed as a result of the shock. Therefore they could not confirm the shock theory of Penner.

At this point one might conclude that prior to 1950 this disease was recognized only on the surgical wards; it is also true that most of the previously mentioned cases were preceded by abdominal surgery. However, in 1952, Kleckner et al.⁶ reviewed the clinical and pathological findings in 14 patients who had not had abdominal surgery. The process was considered the immediate cause of death in seven of the 14 cases. The autopsy findings were the same as those noted in the postoperative cases. All of the patients reported manifested circulatory collapse, but it could not be determined whether this preceded or followed the onset of the intestinal lesion. No increase was noted in the incidence of the disease since antibiotics had been used for the treatment of intestinal lesions. It was, therefore, concluded that the use of such drugs could not be implicated in the pathogenesis of the entity.

Pettet et al.⁷ described 94 patients who died in the postoperative period with extensive pseudomembranous involvement of the gastrointestinal tract at the Mayo Clinic during the period 1925-1953. It was interesting to note that prior to 1948 there were no instances of correct ante-mortem diagnoses in this group; subsequent to that time the disease was correctly diagnosed in 14 of 26 cases. These workers could demonstrate no significant increase in the incidence of the disease since the advent of antibiotics. There were 45 cases found before, as opposed to 49 cases noted after antibiotics became available. Forty-four percent of the patients in the study had carcinoma of the colon. Although the investigators were unable to find any one etiologic factor, it was thought that the incidence of colon carcinoma was of significance. Importance was also attached to the observation that 71 of the 94 patients had some type of infectious process, usually pneumonia or peritonitis. Some of the patients seen during the latter part of the study had large numbers of staphylococci in culture of feces at necropsy. These organisms were quite resistant to the usual antibacterial drugs. It was, therefore, suggested that a change in the normal balance of the intestinal flora may have been important. In this series shock was noted after the onset of the abdominal symptoms and was, therefore, considered secondary to, rather than productive of, the intestinal lesion.

Clinical Course

The triad of symptoms which may be helpful in recognizing the onset

of this process consists of: (1) Elevated temperature, (2) abdominal distention and/or diarrhea, and (3) shock.⁸ The most significant clinical features are the sudden onset of profound circulatory collapse which is resistant to the usual supportive measures, and the presence of watery diarrhea.⁶

An often-seen pattern consists of a relapse noted after an initial period of improvement in a patient being treated with antibiotics for various diseases.⁹ There may be a sudden rise in temperature after an afebrile period. The rapid onset of lethargy, mental aberrations, nausea, vomiting, abdominal distention, diarrhea and collapse are characteristic.^{2,9} In the surgical patient the average time of onset is three days post-operatively, although Pearce¹⁰ noted a range of two to 12 days. The diarrhea is not invariable but usually consists of the explosive onset of watery-green or yellow-brown stools. The absence of diarrhea is attributable to adynamic ileus as well as to the sudden onset of the disease which may result in severe outpouring of fluid material into the intestinal lumen with marked dehydration, collapse and death before the diarrhea can occur.

Pain is not a prominent feature, but in those who develop this symptom it ranges from mild discomfort to severe cramps.¹¹

Pathology

The site of involvement of this disease may be anywhere in the G.I. tract but the lesions are found most frequently in the small and large intestine. Of the 94 patients studied by Pettet, 44 had small intestine involvement, 24 small and large intestine involvement, and 12 large intestine lesions.

The Pseudomembrane

At autopsy the intestinal tract is usually greatly dilated and filled with liquid feces. The mucosal surface is generally lined with a friable yellow-green or tan, sticky pseudomembrane that occurs either in isolated plaques or as an extensive process involving several feet of intestine. It is usually readily separated from the underlying mucosa which may be normal or diffusely injected.

Microscopically the membrane consists of a mixture of necrotic cellular debris, fibrin and a variable number of inflammatory cells and mucus, which forms as a result of fibrinoid necrosis of the superficial mucosa. Simultaneously the subjacent glandular structures secrete an excessive amount of mucus. The exudate and the necrotic superficial zones of mucosa coalesce to form the membrane. As the disorder progresses the entire mucosa undergoes coagulative necrosis, and at this stage the membrane may slough, leaving an ulcer with a pyogenic surface which may subsequently penetrate the muscle coat. The submucosa is congested and edematous and may have deposits of fibrin in it, but rarely is there much leucocyte infiltrate, although phagocytes may be quite numerous. In Dearing's^{12,25} study involving a comparison of those cases in which *S. aureus* was cultured at autopsy with those cases in which the organism could not be cultured, there were no demonstrable gross or histologic differences in the intestinal lesions.

Continued

Histologic Sequence

McKay and his group¹³ were able to produce pseudomembranous enterocolitis experimentally in dogs by the administration of incompatible blood into the aorta with concomitant surgical trauma. They traced the histological sequence of events and noted: (a) the earliest changes consisted of thrombosis of the capillaries which initially was not accompanied by necrosis; (b) shortly thereafter the mucosal tissue infarcted with hemorrhage into the connective tissue of the villi and into the lumen; (c) subsequently the mucosal surface was covered with a layer of necrotic tissue from the infarcted superficial mucosa, fibrin, mucus, red blood cells and leukocytes.

In the experimental situation the thrombi appear practically instantly. The development of necrosis is a very rapid process and was observed in one animal two and one-half hours after the incompatible transfusion was started.

Etiologic Factors

In a discussion of the etiology of this disease in 1956, Prohaska et al.¹⁴ suggested that it was incorrect to associate pseudomembranous enterocolitis exclusively with abdominal operations or the use of intestinal antibiotics. Reference was made to the available literature regarding the occurrence of the disease after operations on the brain and breast as well as its occurrence without associated use of antibiotics.

*Staphylococcus Aureus*¹⁴

(1) Pseudomembranous enterocolitis is an infectious disease produced by *S. aureus*. This contention was felt to be supported by the large number of cases in the world literature in which staphylococci were isolated in pure culture. (2) *S. aureus* does not establish itself in the intestinal tract containing the usual bacterial flora, as evidenced by the work of Dack who, in his studies on food poisoning, was seldom able to recover staph in the stools of volunteers who took the microbe by mouth. (3) Shock and the fatal course of the disease are enhanced by micrococcal enterotoxin. This was supported by experiences with the enterotoxin in the majority of strains of staph associated with fatal pseudomembranous enterocolitis. (4) The effect of the enterotoxin may be negated by the administration of ACTH. In this regard the group reported their experiences in two patients who had the diagnosis confirmed at laparotomy and then had dramatic response to ACTH. It is interesting that in an earlier publication discussing this mode of therapy Prohaska stressed the importance of differentiating staph enteritis from pseudomembranous enterocolitis since the former might respond adversely to the drug. "Any bacterial disease would have been markedly aggravated by corticotropin . . . we believe therefore, that the disease is not an infection."¹⁵

The frequent recovery of staphylococci from the diarrheal stools of patients with this clinical diagnosis has led others to conclude that the organism is causally related to the disease. Bockus² indicates that greater than 50 percent of authenticated cases of pseudomembranous enterocolitis have been attributed to staphylococcal infections in association with antibiotic therapy. It has been suggested that the organism was not cultured prior to 1950 because the media used were selective for intestinal pathogens and were not suitable for growth of staphylococci.⁷

Antibiotics

There is adequate documentation in the literature that this entity was recognized as a postoperative complication long before the advent of antibiotics.¹ However, reports vary as to the change, or lack of change, in incidence of the disease with the recent increased use of broad-spectrum antibiotics.

The exact relationship between broad-spectrum antibiotics and pseudomembranous enterocolitis is not clear. It is well known that such antibiotics can produce a change in the intestinal flora with suppression of normal bacteria and associated increased growth of resistant organisms such as staphylococci in the colon. However, the mechanism of production of the distinct lesion is obscure, particularly in the small intestine which is usually almost entirely free of bacteria.¹⁷

The possibility of an infective etiology is in part suggested by the experimental production of pseudomembranous enterocolitis in chinchillas by the oral administration of staphylococci or enterotoxin or both in association with antibiotic therapy.¹

Dearing¹² showed that fatal pseudomembranous enterocolitis may occur both with and without culturable *Staphylococcus aureus* in the intestinal tract and that severe staphylococcus enteritis may exist without pseudomembranes in the intestine. He emphasized that although fatal pseudomembranous enterocolitis may occur in patients who have not received antibiotics prior to or during the course of their enteritis, patients with staphylococcus enteritis almost always have received antibiotics which affect the intestinal flora in such a way that the growth of staphylococcus is encouraged.

Several years ago Palmer¹⁹ suggested that too much blame had been placed on antibiotics in the etiology of this disease. He thought that although the proliferation of virulent staphylococci might add to the surface damage, the basic cause of the process was probably related to factors which depressed the intrinsic mucosal vitality. He presumed a hypoxic process to be the most likely etiology and suggested a local vascular fault as being responsible for the sudden infarction of many feet of mucosa with sparing of the deeper tissue.

Shock

Birnbaum¹ reviewed 40 cases diagnosed at autopsy and found that in all cases there was a concurrent problem with either shock, anemia, heart failure, hydrothorax or an inflammatory pulmonary condition. He pointed out that all of these factors are likely to lead to hypoxia, which may well have been the common factor involved.

Markley et al.²⁰ reviewed 14 cases with a diagnosis of pseudomembranous enterocolitis made at post-mortem examination. These cases demonstrated in varying frequency many of the associated factors that are often ascribed etiological significance, including shock, surgery, previous antibiotic therapy, staphylococcal infections, intestinal obstruction. The reviewers concluded that none of these factors occurred with sufficient preponderance to suggest a constant causal relationship. It was suggested that the common denominator in these cases consisted

Continued

of an impairment of the blood supply of the intestine. The workers attached significance to the finding that in those cases with localized ischemia, the areas with most severe pseudomembranous involvement were those adjacent to the ischemic bowel, although other portions were also involved. It was concluded that "the evidence at hand indicates that pseudomembranous enterocolitis is a pathologic entity resulting from the action of a variety of noxious factors in the presence of an underlying disorder characterized by a deficiency in the volume of blood or in the nutrient quality of the blood reaching intestinal tissue."

Although this is a logical conclusion on the basis of their series, it is unlikely that this represents an essential condition in all cases, since this entity has been demonstrated in children without vascular abnormality or mechanical embarrassment of intestinal blood flow.

Intravascular Coagulation

In the experimental production of the disease in dogs, McKay and his coworkers concluded that the trigger mechanism involved was an episode of intravascular coagulation and that the pseudomembrane was caused by thrombi in the mucosal capillaries. The localization of the thrombi in the intestine was explained by "compensated shock" which was due to the surgical trauma and the concomitant pooling of blood in the splanchnic capillary bed. The pathology of the lesions was considered identical to that found in man; however, the authors readily admitted that there was uncertainty as to the extent of applicability of these experiments in the clinical syndrome.

In a follow-up report these investigators²¹ indicated that the experimental production of these lesions could be prevented with preheparinization of the animals. They suggested that the syndrome resulted from two distinct phenomena: (1) "circulatory collapse," assumed to be produced by intravascular coagulation in submucosal shock and usually occurring postoperatively. Antibiotics may or may not have been used. Diarrhea is not necessarily present. Mortality is high in this group. (2) A "diarrhea type" resulting from alteration of the intestinal bacterial flora with the predominant growth of staphylococci and the development of staphylococcal enteritis. This type may or may not have been preceded by surgery and is most often associated with antibiotic therapy. Shock is said to develop more gradually in these cases, and the mortality is low in adequately treated patients.

The authors concluded by proposing that a combination of bacterial enteritis and capillary thrombi may actually be the most common etiology of this phenomenon.

Obstructive Mechanism

Hale and Cosgriff¹¹ have discussed a variety of possible etiological mechanisms, including a suggestion by Pettet that obstruction of the G.I. tract may be of significance in that the resulting alteration of permeability of the bowel wall could predispose to invasion by pathogenic microbes. Another possible mechanism suggested is that pseudomembranous enterocolitis may represent a local tissue reaction similar to the Shwartzman phenomenon.* Sensitivity of the patient to the

*See Test Your Word Score Page 363.

antibiotic is another consideration. It is thought that this would best explain cases in which the syndrome develops a few hours after administration of the drug.

A review of the possible etiologies was perhaps best summed up by Baggenstoss⁷ in 1954 when he stated ". . . there are probably many causes of this lesion. The manner in which the intestinal mucosa can react to injury is limited; formation of a pseudomembrane probably can be brought about by a wide variety of toxic and infectious agents. Consequently one set of factors may have been operative in the pre-antibiotic period and now a different set of factors may be responsible."

The confusion regarding the etiology of the lesion stems from the variety of circumstances under which it is noted.¹⁴ It may be found with and without surgery, with and without antibiotics, and with and without staphylococci. It is difficult to conceive of the disease as a distinct entity until the opposing factors are made to fit into some pattern that encompasses all variations.

Diagnosis

Sudden Diarrhea

This diagnosis should be considered in any patient receiving antibiotic therapy who develops diarrhea and fever. Sudden dehydration in these patients should suggest loss of fluid into the bowel, if there is no diarrhea. There is no other pathologic entity, with the exception of cholera, that produces such profound shock and dehydration as pseudomembranous enterocolitis.

Increase of Gram-Positive Cocci

A smear of stool showing a relative increase in gram-positive cocci helps to confirm the diagnosis in those cases in which staphylococci are associated. Hale and Cosgriff have indicated that sigmoidoscopy may reveal the typical membranous involvement; a smear taken from the lesion may reveal organisms that were not detected on the routine smears. The diagnosis is particularly difficult in the postoperative patient, since surgical complications may be responsible for the gastrointestinal symptoms. There are no pathognomonic clinical or radiologic findings.

Radiologic Findings

In the series studied by Feinberg²² the radiologic findings were primarily limited to the small intestine and generally suggested incomplete or complete obstruction. Persistence of the distended intestinal loop or loops for days, or until death, constituted the most striking finding and emphasized the challenge of excluding obstruction by roentgenologic means. Awareness of the possibility of the lesion and a high index of suspicion are of the utmost importance, since early therapy may be life-saving. In Pearce's study¹⁰ it was noted that in three patients who recovered there was an average interval of 5.7 hours from the initial manifestations to therapy; whereas in those cases ending fatally and recognized clinically there was an average of 40 hours before the disease was suspected and treatment begun.

Continued

Treatment

Because of the frequent isolation of staphylococci in cases of pseudomembranous enterocolitis, therapy of the entity is usually discussed with relationship to this organism.

*Therapeutic Outline*²³

1. Discontinuance of present antibiotics.
2. Specific antistaphylococcal antibiotic therapy.
3. Hydration (I.V. fluid).
4. Blood transfusions to combat shock in severe form.
5. Vasopressors and steroids to combat shock in severe form.
6. Fecal enemas. Some workers are dubious of the efficacy of this mode of therapy in restoring normal bowel flora. Altemeier indicates that esthetic as well as clinical problems preclude its routine use.
7. *Lactobacillus acidophilus*. This is a normal intestinal inhabitant which has been made resistant to commonly used antibiotics. It helps restore the normal flora and eliminate staphylococcal overgrowth.
8. Paregoric, kaopectate, etc.

Antibiotics

It is well known that as new antibiotics are introduced, several months elapse before resistant strains of *S. aureus* are noted. Such organisms initially appear sporadically and then may finally become established in the hospital depending upon the usage of the antibiotics. Erythromycin and chloromycetin-resistant strains are being encountered more frequently.¹⁸

At present such newer penicillins as sodium oxacillin and methicillin are considered the antibiotics of choice by some workers. Wallace et al.²⁴ report that vancomycin has been uniformly effective in terminating diarrhea and eliminating staphylococci from the stool, usually within 48-72 hours after institution of therapy. The suggested dose is 0.5 gm. p.o. q6h until the diarrhea ceases.

Summary

The pathogenesis and etiology of pseudomembranous enterocolitis remain obscure. Many workers² discuss this disease and staphylococcal enterocolitis as the same entity or as a variant of the same entity. Others strongly advocate a separation of the two into distinct disorders.¹² A review of the literature reveals a frequent association between the pseudomembranous disorder and the recovery of staphylococci from the diarrheal stool. However, the basic mechanism or underlying disorder has not yet been elucidated. Theories in this regard include hypoxia, local vascular defects, increased permeability of the intestinal wall with resulting bacterial invasion. Although staphylococci may be a factor in accentuating or producing some of the cases of pseudomembranous enterocolitis, it does not adequately explain all occurrences.²⁵

Case Report

History

A 50-year-old chronic alcoholic was admitted to the Hennepin County General Hospital for the third time on 4/19/66 with a one-week history of cough and dyspnea. The cough had been productive of greenish sputum for three days prior

The answer may be yes...if they're not on Hygroton. For instance, a therapeutic dose of a short-acting diuretic may cost 3 times as much as an equivalent dose of Hygroton. With Hygroton, in fact, you can usually do the job with just one tablet a day or one every other day. It's no wonder that the trend has been away from short-acting, multiple-dose, high-cost diuretics.

You may hear that a short-acting diuretic was more effective in a 400 mg. (ten-tablet) dose than Hygroton in a 200 mg. (two-tablet) dose.

If one considers maximum recommended doses for each product, tablet for tablet Hygroton was clearly superior. Two tablets of Hygroton were found to produce almost 40% more natruresis and 20% more weight loss than five tablets of the other diuretic.* Note that these are maximum recommended doses!

For effectiveness, economy, and convenience, therefore, Hygroton is the diuretic to choose to start with and the one to stay with.

*Brest, A. N., et al.: J. New Drugs 5:329, 1965.

Natruresis above control values after maximum recommended doses (mEq./24 hours) in "normal" patients	
111	152
5 tablets short-acting nonthiazide diuretic	2 tablets Hygroton
48-hour weight loss after maximum recommended doses in edematous patients with congestive heart failure due to arteriosclerotic or rheumatic heart disease	
1.84 lbs.	2.2 lbs.
5 tablets short-acting nonthiazide diuretic	2 tablets Hygroton

Indications: Hypertension and many types of edema involving retention of salt and water.

Contraindications: Hypersensitivity and most cases of severe renal or hepatic disease.

Warning: With administration of enteric-coated potassium supplements, the possibility of small bowel lesions should be kept in mind.

Precautions: Reduce dosage of concomitant antihypertensive agents by at least one-half. Discontinue if the BUN rises or liver dysfunction is aggravated. Electrolyte imbalance and potassium depletion may occur; take special care in cirrhosis or severe ischemic heart disease, and in patients receiving corticosteroids, ACTH,

or digitalis. Salt restriction is not recommended.

Side Effects: Dizziness, weakness, nausea, vomiting, hyperglycemia, hyperuricemia, headache, muscle cramps, postural hypotension, constipation, leukopenia, thrombocytopenia, agranulocytosis, impotence, dysuria, transient myopia, skin reactions, including urticaria and purpura, epigastric pain, or G.I. symptoms after prolonged administration.

Average Dosage: One tablet (100 mg.) with breakfast daily or every other day.

Availability: Tablets of 100 mg. in bottles of 100 and 1000. For full details, see the complete prescribing information. 6524-V(B)

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to admission but had changed to rusty color the day of admission. Because of increasing respiratory difficulty he came to the Emergency Dept. for admission.

Significant past history included hospitalization at Glen Lake Sanatorium in 1962 for active pulmonary tuberculosis.

Physical examination revealed a tremulous, elderly white male in moderate respiratory distress. Temperature was 101.8 rectally. Blood pressure 100/70. Pulse 180. Chest, dullness to percussion at right base, inspiratory rales at right base. Abdomen unremarkable. Rectal examination unremarkable. Skin, marked subcutaneous emphysema in the head and neck region.

Laboratory Data

Chest x-ray, massive right lower lobe infiltrate, pneumomediastinum and small left pneumothorax. EKG, supraventricular tachycardia. Sputum smear, gram-positive diplococci. Sputum culture, pneumococci. Blood culture, pneumococci. Hemoglobin 15.0; white blood count, 12,300; 96% neutrophils; 4% lymphocytes.

Hospital Course

Because of a penicillin allergy, therapy was initiated with erythromycin, 500 mgm. I.V. q6h. He remained strikingly dyspneic and acutely ill. A chest catheter was inserted to alleviate the small pneumothorax, but there was no significant improvement. On the fourth hospital day the patient vomited and became apneic. He responded adequately to intubation and subsequent tracheostomy. Because of the possibility of aspiration, chloromycetin, 500 mgm. q6h I.V., was added to his therapy to provide broader coverage. On the sixth hospital day he began having frequent loose green stools. Two days later he suddenly developed increased respiratory difficulty, fever of 104 degrees, hypotension, abdominal distention, and a venous pressure of 0.5 cm. of water. His urine output decreased from 200 to 300 cc. q4h to 30 cc. q4h. Stool cultures which had been obtained two days previously revealed numerous *Staphylococcus aureus*, coagulase positive, which were sensitive to chloromycetin but resistant to erythromycin. He responded dramatically to vigorous parenteral fluid therapy. During succeeding days he continued to excrete large quantities of turbid green stool. A repeat culture revealed staphylococci which were resistant to chloromycetin and erythromycin. Therapy consisted of parenteral fluids, including plasma and whole blood; fecal enemas, *Lactobacillus acidophilus*, vancomycin orally, keflin parenterally, and discontinuance of erythromycin and chloromycetin. The patient gradually improved, such that treatment for the gastrointestinal difficulty could be discontinued by the 13th hospital day. During the remaining two weeks of hospitalization, attention was devoted to the treatment of his lung disease. There was no recurrence of the gastrointestinal symptoms. Repeat stool cultures revealed no pathogens. He was discharged and is being followed in the outpatient department.

References

1. Birnbaum, D., Laufer, A., Freund, M.: *Gastroenterology* 41:345, 1961.
2. Bockus, H. D.: *Gastroenterology*, Vol. II, 2nd Ed., p. 799, W. B. Saunders Co., Philadelphia, 1964.
3. Speare, G. S.: *Amer J Surg* 88:523, 1954.
4. Penner, A., Bernheim, A.: *Arch Path* 27:966, 1939.
5. Dixon, C. F., Weismann, R. E.: *Surg Clin N Amer* 28:999, 1948.
6. Kleckner, M. S., Borgen, J. A., Baggenstoss, A. H.: *Gastroenterology* 21:212, 1952.
7. Pettet, J. D., Baggenstoss, A. H., Judd, E. S., Dearing, W. H.: *Proc Mayo Clin* 29:342, 1954.
8. Cruz, Horacio: *Amer J Proctol* 12:176, 1961.
9. Newman, C. R.: *Ann Intern Med* 45:409, 1956.
10. Pearce, C., Dineen, P.: *Amer J Surg* 99:292, 1960.
11. Hale, H. W., Cosgriff, J. H.: *Amer J Surg* 94:710, 1957.
12. Dearing, W. H., Baggenstoss, A. H., Weed, L. A.: *Gastroenterology* 38:441, 1960.
13. McKay, D. S., Hardaway, R. M., Wahle, G. H., Hall, R. M.: *Arch Intern Med* 95:779, 1955.
14. Prohaska, J. V., Long, E. T.: *Arch Surg* 72:977, 1956.
- 15-25 May be secured from Grand Rounds Editor.

Two things we ought to learn from history: one, that we are not in ourselves superior to our fathers; another, that we are shamefully and monstrously inferior to them, if we do not advance beyond them. — T. Arnold



Book Reviews

What sculpture is to a block of marble, education is to the human soul. The philosopher, the saint, the hero, the wise, and the good, or the great, very often lie hid and concealed in a plebeian, which a proper education might have disinterred and brought to light. — Addison

MEDICAL PHARMACOLOGY, PRINCIPLES AND CONCEPTS — 3rd Edition, By Andreas Goth. Publication date: January 25, 1966, The C. V. Mosby Co., \$12.50.

This book suffers from its virtues. The author aims to provide a "concise text containing the principles and concepts of modern pharmacology" in a book "of modest size." He achieves saving of space by "selectivity and conciseness," and he tries to avoid the danger of "too many details which may obscure for the student or practitioner what is really exciting about those areas of pharmacology that are expanding and are contributing greatly to modern medicine."

For the practitioner who is interested in one of the areas discussed in this book, the concise presentation permits him to gain a good knowledge of the clinical pharmacology in that area. Eleven sections of the book are entitled: (1) General Aspects of Pharmacology, (2) Drug Effects on the Nervous System and Neuroeffectors, (3) Psychopharmacology, (4) Depressants and Stimulants of the Central Nervous System, (5) Anesthetics, (6) Drugs Used in Cardiovascular Disease, (7) Drug Effects on the Gastrointestinal Tract, (8) Drugs That Influence Metabolic and Endocrine Functions, (9) Chemotherapy, (10) Poisons and Antidotes, and (11) Prescription Writing and Drug Compendia. The presentation in each section is "concise", but a bibliography for each chapter contains a grouping of recent review articles so that the interested reader can find more detailed information if he has need. The reviewer's concern, however, may be unwarranted; for demand of a second and now a third edition of this book by students and practitioners suggests that many of them agree with the author's statement that "conciseness is a necessity — for a book that is to be used by over-burdened students and physicians." In a field as vast as clinical pharmacology conciseness in writing is a necessity for all authors, and the real choice is between selective and attempted comprehensive presentations. If the choice is "selective" and the areas of interest lie within this book, the purchaser will be satisfied. If not, there is always Goodman and Gilman.

Warren J. Warwick, M.D.
Minneapolis, Minnesota

PROGRESS IN CLINICAL CANCER — Irving M. Ariel, M.D., Grune and Stratton, New York-London. 375 pages, \$15.75.

Ariel has again accumulated an excellent set of manuscripts dealing with the advances in clinical cancer. In that the book is dedicated to Owen H. Wangenstein, most of the authors have been previous students of his who are now scattered from the east coast to the west coast.

Some of the new techniques of diagnosis, surgery, and irradiation are interesting and enlightening phases of this monograph. Though this book would be of interest to the advanced student, it serves its best purpose for the surgeon who is interested in the problem of tumors, their diagnosis and treatment.

Carl O. Rice, M.D.
Minneapolis, Minnesota

CURRENT PRACTICE IN ORTHOPAEDIC SURGERY — September 1966, Volume 3. Adams, C. V. Mosby, \$18.75.

The third volume of this rather compact and well-constructed text differs somewhat from the previous two volumes in that it is slanted even more to topics of pure orthopaedics. A new section on history adds interest to the book. The second section relates to the application of certain orthopaedic procedures in the management of patients with cerebral palsy. The last section is on general orthopaedic procedures, including a very scholarly dissertation on the use of multiple pins in femoral neck fractures and the importance of two-plane reduction, total impaction, and absolute fixation.

The subject matter is well written, although improvement could be made in the anatomical illustrations; fortunately, they are few. The book should appeal to the resident in orthopaedics and to the specialist himself.

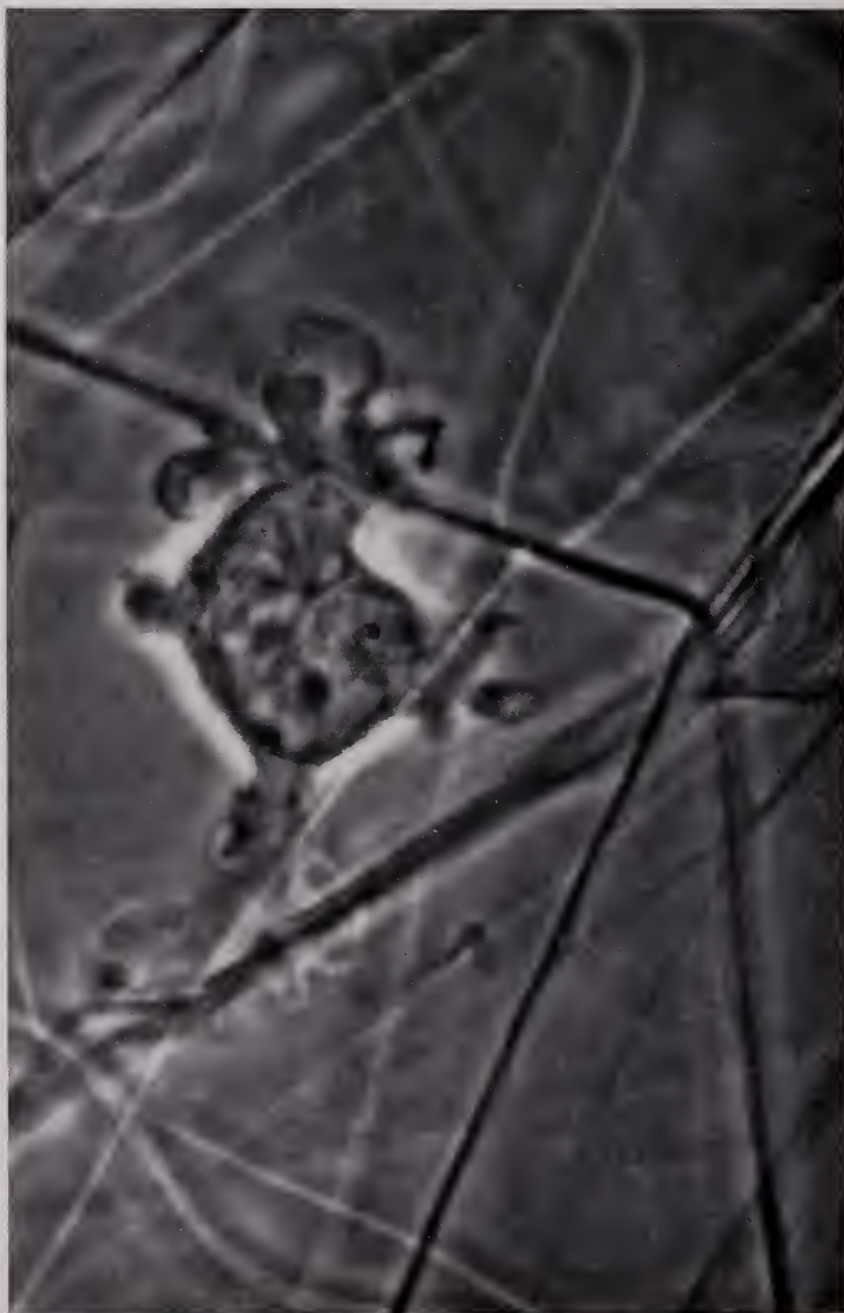
Harrison H. Farley, M.D.
Minneapolis, Minnesota

INFLAMMATION: A cellular fight for life

A SYNTEX REPORT based on recently developed hypotheses about topical corticosteroids, including the cellular theories of inflammation by Thomas F. Dougherty, Ph.D., University of Utah.

You are looking at a fibroblast fighting for life. This cell—one of the most common found in connective tissue—has literally been poisoned by cytotoxins released from other cells that have ruptured. Soon, if the abnormal activity of this fibroblast does not cease, it, too, will rupture and die—one more casualty in the inflammatory wave of destruction precipitated by injury.

Until a short time ago no one had ever witnessed such a scene at the cellular level. Now, through advanced cinemicrographic techniques, it is possible to view and photograph the inflammatory process as produced experimentally in living animal tissue. This method permits new insight into the mechanism of inflammation and the role of corticosteroids in therapeutic management. Equally important, these techniques shed new light on factors that may make one corticosteroid more effective than another—factors that can be correlated with other chemical, biologic, and clinical parameters.

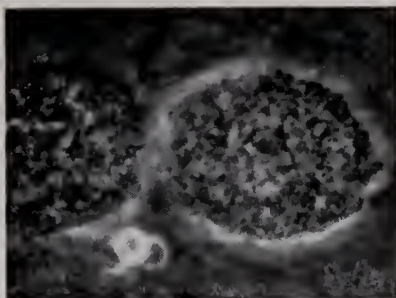


Visual evidence of how corticosteroids influence the inflammatory reaction

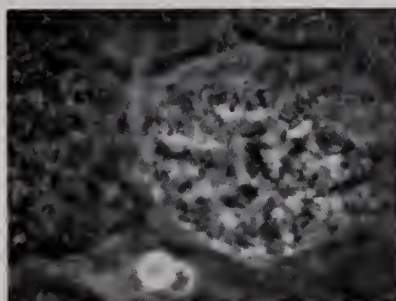
Working with phase-contrast cine-micrography on living animal tissue, Doctors Thomas F. Dougherty and David Berliner of the University of Utah College of Medicine have actually filmed cellular events that occur during the inflammatory reaction. This remarkable study* and additional work by these investigators, as well as by others, have established a new theoretical biologic basis for the antiinflammatory effect of the corticosteroids. (It must be noted that other theories, such as the lysosome or so-called "suicide bag" theory, have been postulated, although it is quite likely that there are more similarities than differences among the various theoretical models.)

The inflammatory wave of destruction

In this investigation an injurious injection of gelatin is used to set off an inflammatory reaction in living mouse tissue. What follows is a wave of destructive cellular activity that comprises the inflammatory response to injury. Mast cells (which contain heparin, serotonin and histamine) take up water, swell and rupture, releasing their contents, which are toxic outside the mast cell wall. These toxins, in turn, cause disintegration of other cells (such as fibroblasts) and the release of additional toxic material. Capillaries, too, take up water and leak unformed blood elements, causing edema. And polymorphonuclears, lymphocytes and perithelial cells invade the inflamed site. As a result of all these changes, the cellular environment reaches a state of turmoil.



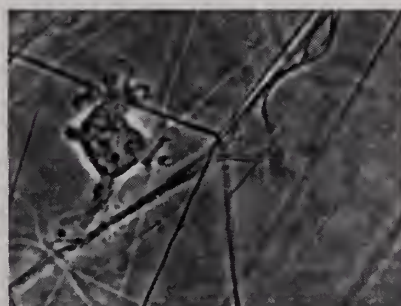
Phase-contrast microscopy showing mast cell before injury.



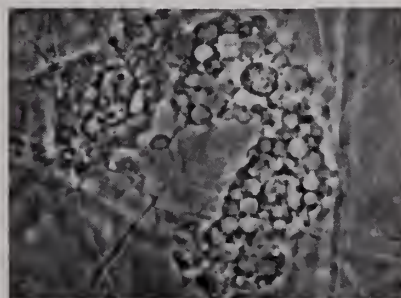
Mast cell (after injury) has broken up and released cytotoxins.

How corticosteroids change the picture

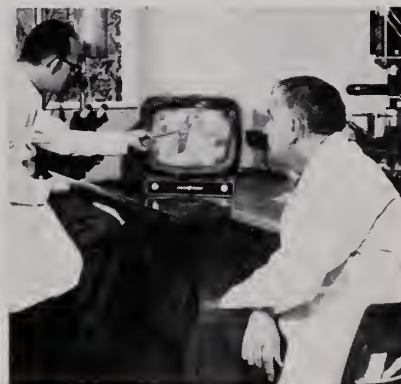
Corticosteroids appear to virtually stop the abnormal cellular activity that constitutes the inflammatory reaction. This permits the body's natural resources to clear up the inflamed area and repair the damaged tissue. This interpretation is supported by the fact that when the injurious gelatin solution is injected simultaneously with a corticosteroid—Synalar (fluocinolone acetonide)—the inflammatory pattern simply does not develop.



Fibroblast in high state of activity, much distorted.



Mast cells showing effects of corticosteroid action: cells are normal in size, shape and activity.

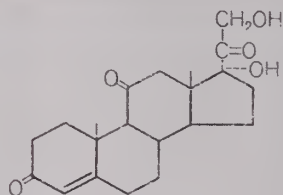


In summarizing his study Doctor Dougherty states: "...we also feel this work may explain why one corticosteroid helps a patient more rapidly and effectively than another. If it does, it is because one corticosteroid is the fastest, most effective inhibitor of the series of inflammatory events at the tissue level."

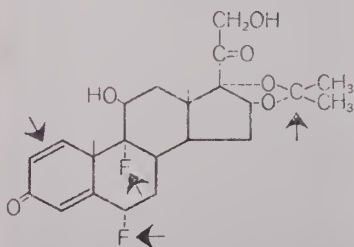
*A New View of Corticosteroid Action in Inflammatory Dermatoses, a film based on this study, is now available from your Syntex representative.

How advances in chemical design have achieved greater steroid potency

The chemical modification of corticosteroid molecules from the advent of hydrocortisone to the development of Synalar (fluocinolone acetonide) is a prime example of how biochemists can "design" to increase therapeutic activity and minimize undesirable side actions. Below, for example, we see the important changes that were made in reference to the hydrocortisone molecule to produce fluocinolone acetonide, one of the most active of all topical corticosteroids. As a result, a 0.01% preparation of Synalar (fluocinolone acetonide) has been reported to do the work of a 1% hydrocortisone product containing 100 times more corticosteroid. And it can often do it more effectively.



Hydrocortisone

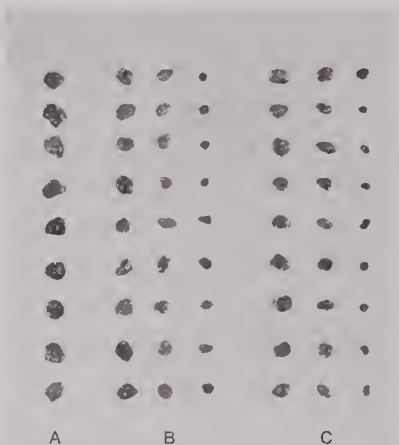


Fluocinolone Acetonide (Synalar)

- ☐ a double bond between carbons 1 and 2
- ☐ fluorine substitutions at both the 6- α and the 9- α positions
- ☐ the addition of the acetonide at the 16- α , 17- α positions, thus providing one of the most potent topical corticosteroids available.

How bioassay tests are used to "predict" therapeutic potential

Biologic assays are another tool used by researchers to help establish the relative activity of corticosteroids. To date no single method of assaying corticosteroid activity has emerged as the ideal "yardstick" for predicting therapeutic potential. Taken together, however, these methods have proved useful. When such tests are run on various corticosteroids, a definite order of corticosteroid activity becomes evident. Compounds with the highest order of activity may be expected to merit clinical trial to establish their high therapeutic potential. When assayed by these methods, fluocinolone acetonide (Synalar) emerges as one of the most active topical corticosteroids, milligram for milligram, available for clinical application today.



THE THYMUS INVOLUTION ASSAY¹⁻⁴ is run on adrenalectomized rats. The sizes of the glands are measured, and the degree of involution caused by the steroid is determined as an indication of its potency. In the above photo, the comparative involution of thymus glands achieved with hydrocortisone and Synalar (fluocinolone acetonide) is shown. Untreated controls (A) show normal size. Group B— injected with 1, 2 and 4 mg. of hydrocortisone—show progressively smaller thymuses as does Group C— injected with fluocinolone acetonide—but with only 1/500th the dose of hydrocortisone.



THE ANTIGRANULOMA ASSAY¹⁻⁴ also utilizes adrenalectomized rats. Granulomas are induced by subcutaneous implantation of cotton pellets on either side of the thorax. The degree of granuloma inhibition achieved by a steroid reflects its potency. The above photo shows the inhibition of granuloma formation achieved with hydrocortisone and Synalar (fluocinolone acetonide). Untreated controls (A) show large, red granulomas adhering to the pellets. Group B, receiving hydrocortisone and Group C, receiving fluocinolone acetonide, show little, if any, granuloma formation. Fluocinolone acetonide produced the same effect as hydrocortisone with only 1/500th the dose. This assay, as well as the thymus involution assay, measures systemic rather than topical corticosteroid activity. Nevertheless, results by these methods correlate well with other assays and with the milligram potencies of topical steroids in current clinical use.

Worldwide clinical experience confirms the predictable therapeutic potential of Synalar

It is particularly gratifying that the promise of the advanced chemical design and high order of bioassay activity of Synalar (fluocinolone acetonide) has been confirmed by widespread therapeutic application. Indeed, the impressive clinical response rate of Synalar has been documented in no fewer than 232 papers from 22 countries.

PRESCRIBING INFORMATION

For initiation of therapy: Cream 0.025%, 5 and 15 Gm. tubes, 425 Gm. jars; *for emollient effect:* Ointment 0.025%, 15 Gm. tubes; *for maintenance therapy:* Cream 0.01%, 15 and 45 Gm. tubes, 120 Gm. jars; *for intertriginous or hairy sites:* Solution 0.01%, 20 cc. and 60 cc. plastic squeeze bottles; *for infected inflammatory dermatoses:* Neo-Synalar® Cream (0.025% fluocinolone acetonide, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes.

CONTRAINDICATIONS: Tuberculous, fungal, and most viral lesions of the skin, (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. **Contraindicated** in individuals with a history of hypersensitivity to any of the components. **PRECAUTIONS:** Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for pro-

Representative Clinical Results with Synalar*

Efficacy Documented in over 4,000 Patients

Condition	Number of *Publications	Number of Patients	Significant Improvement†
Contact Dermatitis	27	750	713
Eczematous Dermatitis	21	472	409
Seborrheic Dermatitis	18	442	426
Atopic Dermatitis	24	460	426
Psoriasis	36	1,699	1,510
Neurodermatitis	18	351	324
Total	144	4,174	3,808

*Complete bibliography on request.

†Expressed by the authors as excellent, very good, good, complete remission of inflammation, etc.

longed periods of time. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. When severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. **SIDE EFFECTS:** Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. The neomycin in Neo-Synalar Cream rarely produces allergic reactions.

REFERENCES: 1. Lerner, L. J., Bianchi, A., Turkheimer, A. R., Singer, F. M., and Borman, A.: Anti-inflammatory steroids: potency, duration and modification of activities. *Ann NY Acad Sci* 116:1071 (Aug. 27) 1964. 2. Idem: Comparison of anti-granuloma, thymolytic and glucocorticoid activities of anti-inflammatory steroids. *Proc Soc Exp Biol Med* 116:385 (June) 1964. 3. Ringler, A.: Activities of adrenocorticosteroids in experimental animals and man, in Dorfman, R. I.: *Methods of hormone research*, New York, Academic Press, 1964. vol. III. pp. 234-280. 4. Gubersky, V. R.: To be published.

fluocinolone acetonide — an original steroid from

SYNTEX
LABORATORIES INC., PALO ALTO, CALIF.

For inflammatory
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by any measure
a topical corticosteroid
of choice

Synalar® (fluocinolone acetonide)

Milligram for milligram
one of the most active topical
corticosteroids available

Rapid and predictable
in antiinflammatory and
antipruritic activity

Results often comparable to
those of systemic corticosteroids
with fewer hazards

Venereal Disease A Serious National Problem, Says AMA

Venereal disease is spreading so rapidly that it now represents this nation's most urgent communicable disease problem.

VD is hitting particularly hard among teenagers and young adults, according to the American Medical Association.

The venereal diseases are infecting about two Americans a minute—3,000 a day, or 1,100,000 a year. Cases of infectious syphilis have almost tripled in this country in the past five years. More than a million

new cases of gonorrhea are developing annually.

VD can blind, cripple, and even kill.

The ravages of venereal diseases are all needless tragedy, says the AMA, because both syphilis and gonorrhea can be avoided. If contracted, they can be cured by prompt medical treatment.

The cure for both diseases—penicillin—has been available since 1943. Any family physician or public health clinic can administer

prompt treatment.

Venereal disease is caused by intimate personal contact.

Complacency, ignorance, and a free-and-easy attitude toward moral standards are partly responsible for the spread of VD; the increasing use of alcohol, especially among young people, also plays a role.

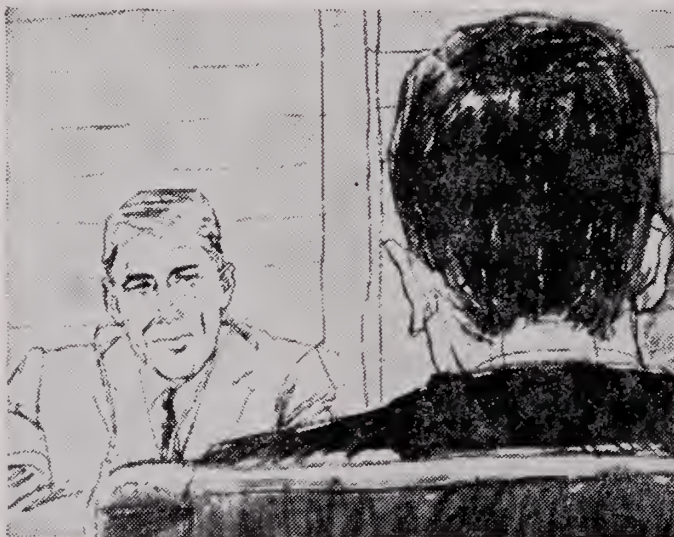
Authorities believe, however, that thousands of young people simply aren't aware of the dangers of VD. Once infected, they are complacent about treatment.

One of the first signs of syphilis may be a painless, ulcerating sore. Gonorrhea produces inflammation of the genital and urinary tracts, and a discharge of pus.

A person may contract syphilis and be unaware that he has the disease. After the first symptoms, the germs may remain hidden in the body for as long as 20 years before any damage is discovered. Then the person may become crippled, develop heart disease, blood vessel disease, blindness, or show mental symptoms. Even death may result from this hidden stage of syphilis.

If left untreated, gonorrhea may be responsible for arthritis, endocarditis, sterility, and blindness.

If a person suspects he may have contracted venereal disease, he should go to a physician immediately.



VD should be treated promptly by a physician.



Abstracts, Briefs and Commentaries

PROLONGED HYPOGLYCEMIA

Two instances of prolonged hypoglycemia precipitated by acetohexamide (Dymelor) in patients with renal failure are reported. In one case, the hypoglycemia persisted for eight days after withdrawal of the drug. Renal retention of acetohexamide metabolites possessing hypoglycemic properties appeared to be responsible for the hypoglycemia. Other published reports are summarized. The author concluded that three mechanisms might explain the prolonged hypoglycemia: (1) decreased glycogen storage secondary to liver disease or starvation, (2) renal damage, or (3) insulinoma. The cause for such an exaggerated effect of the drug is not always apparent.

Clifford F. Gastineau, M.D.*
Rochester, Minnesota

*One of the Contributing, Coordinating Editors of this special issue.

Alexander, R. W.: Prolonged Hypoglycemia Following Acetohexamide Administration: Report of Two Cases With Impaired Renal Function. *Diabetes* 15:362, 1966.

INSULIN-INDUCED HYPOGLYCEMIA

The doctrine that "hypoglycemia begets hyperglycemia" and that excessive doses of insulin are the major cause of instability of diabetes is examined critically in this study.

Four diabetic patients were given 100 gm. of glucose one hour after receiving their usual dose of insulin, and blood sugar values were measured at 30-minute intervals for the subsequent three hours. This procedure was duplicated on another day except that hypoglycemia was produced by the injection of crystalline insulin during the hour before the ingestion of glucose. The impairment of tolerance was no greater following hypoglycemia than during the control observation.

In ten patients, hypoglycemia was produced during the forenoon and recovery was permitted only by the ingestion of the scheduled noon meal. Frequent blood sugar measurements showed no greater postprandial levels than on control days.

The authors conclude that single episodes of hypoglycemia have no significant effect on subsequent blood sugar concentrations when dietary intake is maintained constant. The possibility that frequent repeated

Continued

hypoglycemic episodes could have an adverse effect on the control of diabetes is not excluded.

Clifford F. Gastineau, M.D.
Rochester, Minnesota

Chester, E. M., Travis, R. H., and Mackenzie, M. S.: Lack of Influence of Insulin-Induced Hypoglycemia on Alimentary Hyperglycemia. *Diabetes* 15:307, 1966.

ENZYME STRIP METHOD OF BLOOD GLUCOSE DETERMINATION

Blood glucose levels were determined by an enzyme strip test and by an AutoAnalyzer method in 542 samples. The enzyme strip test tended to overestimate glucose values in the lower ranges and to underestimate them in the upper ranges. A study of the sources of variability showed that the color-matching step appeared to be the source of most of the technical error. The coefficient of variation of independent determinations on 10 samples by four technicians was 27.5%.

The authors conclude that the clinical usefulness of the test is limited and that it should not be used if other methods of determining glucose levels are readily available. These findings, in general, coincide with those published in several British journals. On the other hand, these strips have considerable value in emergency situations, particularly in helping the clinician to distinguish between hypoglycemic and diabetic comas or in distinguishing symptoms of an anxiety attack from those of hypoglycemia. However, the authors specifically state that the strips should not be used for detecting hypoglycemia.

Clifford F. Gastineau, M.D.
Rochester, Minnesota

Hollister, L. E., Helmke, Elizabeth, and Wright, Agnes: Enzyme Strip Method of Blood Glucose Determination. *Diabetes* 15:691, 1966.

TOLBUTAMIDE (ORINASE) FOR TREATMENT OF DIABETES

These authors present the results of nine years' experience with tolbutamide (Orinase) in the treatment of diabetes. They studied 3,387 patients over periods of up to nine years. There were 526 "primary" failures and 202 "indeterminate" failures; 104 of their patients received tolbutamide in combination with other hypoglycemic agents. Among the remaining 2,555 patients, control was satisfactory for at least one month, but 499 of these (approximately 20%) later were not controlled satisfactorily by the tolbutamide and thus were termed "secondary failures." These secondary failures occurred at the rate of approximately 25% per year.

Only about 10% of the patients starting on tolbutamide were known to be taking the drug six to nine years later. Side-effects were few and relatively benign, taking the form of minor skin eruptions and gastrointestinal disturbances which would clear when the drug was discontinued.

There were three instances of blood dyscrasia which could be attributed with reasonable certainty to the tolbutamide. These included thrombocytopenic purpura, nonthrombocytopenic purpura, and neutropenia; these were documented in each instance by tests for circulating antibodies, and in each instance discontinuance of the drug resulted in recovery. No mention was made in this study of the rather common tolbutamide-

induced intolerance to alcohol. Three instances of hypoglycemia were noted.

The authors conclude that tolbutamide and similar agents are valuable adjuncts to the diet therapy of diabetes, although they do have disadvantages in the form of the high secondary failure rate, the possibility that some patients may not regard their problem of diabetes with as much respect as if they were taking insulin, and the frequent reluctance of the patient to accept daily insulin injections later if these should become necessary.

Clifford F. Gastineau, M.D.
Rochester, Minnesota

Balodimos, M. C., Camerini-Dávalos, R. A., and Marble, A.: Nine Years' Experience With Tolbutamide in the Treatment of Diabetes. *Metabolism* 15:957, 1966.

DIABETIC COMA

Twelve instances of coma, occurring in ten diabetic patients and characterized by hyperosmolality and absence of ketosis, are described. The hyperosmolality (>350 mOsm/liter) was the result of either extreme hyperglycemia (936 to 3,120 mg/100 ml. of blood) or hyponatremia (136 to 156 mEq/liter of serum), or of both. The coma itself appeared to be a consequence of the hyperosmolality and cellular dehydration.

This syndrome occurs most often in the elderly person with mild diabetes. The increased blood sugar level usually responds rapidly to doses of insulin which would ordinarily not be adequate for the usual (ketoacidotic) diabetic coma. In some instances, however, several thousand units may be needed. Correction of the hyperosmolality requires administration of large amounts of hypotonic fluids parenterally. Perhaps the most readily available is 0.45% ("half-strength physiologic") saline, but the composition of fluids to be administered should be determined by the chemical findings in the blood at the moment. Potassium is generally needed, as in ordinary diabetic coma.

Epileptiform symptoms were common and were attributed to the extreme hemoconcentration and viscosity of the blood in older patients who already had compromised cerebral vasculature. In two cases, the hematocrit value was more than 90% and the blood resembled syrup.

Seven of these patients died. In the majority of cases, death could not be ascribed solely to the diabetic state but rather to severe complicating disease.

This syndrome characteristically develops rapidly in elderly persons who have mild diabetes, and often there is no apparent reason for the dehydration. Other associated illnesses may appear to provoke these episodes. Similar findings may be encountered with severe burns and with induced hypothermia in nondiabetics, particularly after administration of generous amounts of glucose parenterally. Extreme hyperglycemia without ketosis may complicate hemodialysis when high glucose concentrations in the dialyzing bath are used to reduce edema.

Extreme hyperglycemia and hypertonicity appear to be hazards in themselves. The clinician should be aware of these syndromes and be prepared to carry out appropriate treatment.

Clifford F. Gastineau, M.D.
Rochester, Minnesota

Jackson, W. P. U., and Forman, R.: Hyperosmolar Nonketotic Diabetic Coma. *Diabetes* 15:714, 1966. Knowles, H. C., Jr.: Syrupy Blood. (Editorial.) *Diabetes* 15:760, 1966.

ABDOMINAL ANEURYSM

Operative and nonoperative cases of abdominal aortic aneurysm were studied to determine the effect of resection on long-term survival. Included in the survey were 480 operative and 223 nonoperative cases. The two groups were standardized into subgroups as to age over 70 years, systolic blood pressure over 150 mm. Hg., cardiac status of II, III, IV, blood creatinine level over 2 mg. %, and significant pulmonary disease.

Cumulative survival statistics of the two groups were obtained and curves plotted. Using actuarial methods it was found that removal of the aneurysm with graft replacement approximately doubled the life expectancy.

COMMENT: This is a detailed study. Although there may be valid criticism as to the method used in setting up the study, the striking fact remains that the percentage of deaths by rupture in the nonoperative series is far greater than the percentage due to operative mortality in the comparative group.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

Szilagyi, Emerick D., et al.: Contribution of Abdominal Aortic Aneurysmectomy to Prolongation of Life. *Ann Surg* 164:4:678, 1966.

ELASTOFIBROMA

Pathological curiosities continue to sprout in unexpected places. Pathologists did not identify the elastofibroma, a benign soft tissue tumor of subscapular space, until 1961. Now the reports of Barr and of Brown and his colleagues bring the total of reported cases to eleven.

Barr's communication lists three patients: a forty-five-year old woman with bilateral elastofibromas which occurred four years apart, a sixty-two-year-old woman with a lesion beneath the scapula, and a seventy-five-year-old man with a tumor over the trochanter of the femur. The man's lesion represents the first known instance of an elastofibroma occurring outside the confine of the subscapular space. The report of Brown et al. concerns a fifty-eight-year-old female native of the Ryukyu Islands. She had a 95 by 7 by 6 cm. mass beneath the scapula. The pathogenesis of these curious lesions is uncertain, but they may represent elastotic degeneration of collagen rather than true elastic tissue.

Richard Reece, M.D.
Minneapolis, Minnesota

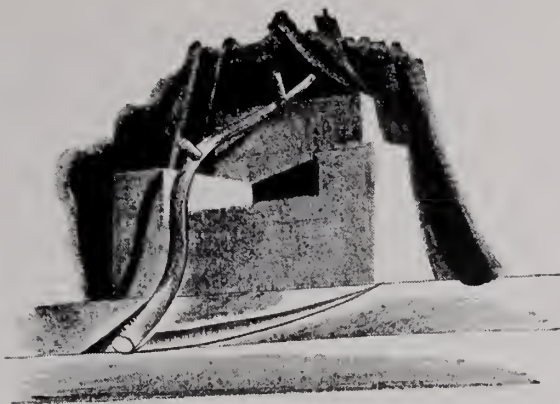
Barr, J. R.: Elastofibroma. *Amer J Clin Path* 45:679, 1966.

Brown, R. K., Clearkin, K. P., Nakachi, K., and Burdick, C. O.: Elastofibroma Dorsi. *New Engl J Med* 275:154, 1966.

Bay Leaves

Bay tree leaves help palsies, convulsions, cramps, aches, tremblings and numbness in any part, weariness also, and pains that come by sore traveling. They wonderfully help all cold and rheumatic distillations from the brain to the eyes, the consumption, old coughes, shortness of breath, and thin rheums.

Nicholas Culpeper



In Memoriam

There are treasures laid up in the heart, treasures of charity, piety, temperance, and soberness. These treasures a man takes with him beyond death when he leaves this world. — Buddhist Scriptures

EDGAR R. SATHER, M.D.

Dr. Edgar R. Sather, 77, prominent Alexandria physician, died December 14, after a short illness. Born in Willmar, Dr. Sather was a graduate of the Iowa State Medical School.

He was a past president of the Park Region Medical Society, a past vice president of the Minnesota State Medical Association and a present member of its Physicians' Assistance Committee, former chief-of-staff of the Douglas County and Our Lady of Mercy hospitals and a member of the American Medical Association. Dr. Sather was also a 50 Club and Life member of the Minnesota State Medical Association.

He is survived by his wife, a daughter and a son.

ARTHUR L. KUSSKE, M.D.

Dr. Arthur L. Kusske, 82, New Ulm physician, died December 31, after a brief illness. Born in Sibley Township, Dr. Kusske received his medical degree from the University of Illinois. He started to practice in Sanborn, Minnesota, in 1907 and for several years made his country calls by horse and buggy. He bought the second automobile sold in Sanborn. Later he practiced in Hutchinson, Minnesota, becoming a specialist in eye, ear, nose and throat.

He was a member of the Brown County Medical Society and American Medical Association and a Life and 50 Club member of the Minnesota State Medical Association.

He is survived by his two sons, Doctors Douglas and Bradley Kusske, eye specialists in St. Paul.

VICTOR M. VAUGHAN, M.D.

Dr. Victor Vaughan, 68, Truman physician, died January 26. Born in Blooming Prairie, Minnesota, Dr. Vaughan graduated from the University of Minnesota Medical School.

He was a member of the Blue Earth Valley Medical Society, American Medical Association and the Minnesota State Medical Association.

He is survived by his wife and one son.

ERNEST A. OLSON, M.D.

Dr. Ernest Olson, 67, Pine Island physician, died January 23. Born in Franklin, Minnesota, Dr. Olson obtained his medical degree at the University of Minnesota Medical School.

In 1965 he was honored by Pine Island on occasion of his having served that community for forty-one years. He was a former president of the Zumbro Valley Medical Society, long-time member of the House of Delegates of the Minnesota State Medical Association, member of the Southern Minnesota Medical Association, American Medical Association, Minnesota Academy of General Practice, and the American Academy of General Practice. He was also on the staffs of the Zumbro Hospital and Olmsted Community Hospital in Rochester.

He is survived by his wife.

ROBERT W. HOLMEN, M.D.

Dr. Robert W. Holmen, 60, St. Paul Otolaryngologist, died February 10. Born in Minneapolis, Dr. Holmen graduated from Gustavus Adolphus College and the University of Minnesota Medical School. After six years in general practice, he entered upon his specialty in otolaryngology and ophthalmology after completing graduate work at the University of Minnesota. He has practiced medicine in St. Paul continuously since 1932 until September of 1966 when he was stricken with his last illness.

He was a director of the Northwest American Medical Association, a member of the Ramsey County Medical Society, American Medical Association, Minnesota State Medical Association and the Academy of Otolaryngology and Ophthalmology. He was on the boards of managers of Bethesda Hospital and the Invalid Home.

Dr. Holmen in addition to his medical practice gave enormous amounts of time to the work of his church. He was a member of the Board of Directors of the Christian Service of the Lutheran Minnesota Conference also serving on many boards, committees and organizations in his church.

He is survived by his wife, a daughter and two sons. His son Douglas is presently stationed in the Middle East with the U. S. Naval Reserve Medical Corps.



TABLETS

Equagesic[®]

(meprobamate and
ethoheptazine citrate with
aspirin)



Precautions: Keep out of reach of children. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate may result in dependence or habituation in susceptible persons—as ex-addicts, alcoholics, severe psychoneurotics. Withdraw gradually after prolonged high dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance. If drowsiness, ataxia or visual disturbances occur, reduce dose. If symptoms persist, caution patients against operating machinery or driving. Give cautiously to patients with suicidal tendencies. Treat attempted suicide with immediate gastric lavage and appropriate supportive therapy.

Side Effects: Ethoheptazine and aspirin may occasionally cause nausea, vomiting, epigastric distress, and rarely dizziness and CNS depression. Overdosage may result in salicylate intoxication. Meprobamate rarely causes allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute non-thrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. Meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioedema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. A few cases of leukopenia, usually transient, have been reported following prolonged dosage. Rarely, cases of aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported; almost always, in the presence of known toxic agents.

Contraindications: History of sensitivity or severe intolerance to aspirin or meprobamate.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.
Wyeth Laboratories Philadelphia, Pa.

Weighing on his mind, too

When pain evokes anxiety and tension, thereby heightening patient discomfort, a simple analgesic may only touch on part of the problem.

This single-prescription, non-narcotic product, however, usually provides effective analgesia *and* helps put the patient's mind at ease.

**Os
frontale**

**Sinus
frontalis**

**Crista
galli**

**Os
nasale**

Lamina cribrosa ossis ethmoidalis

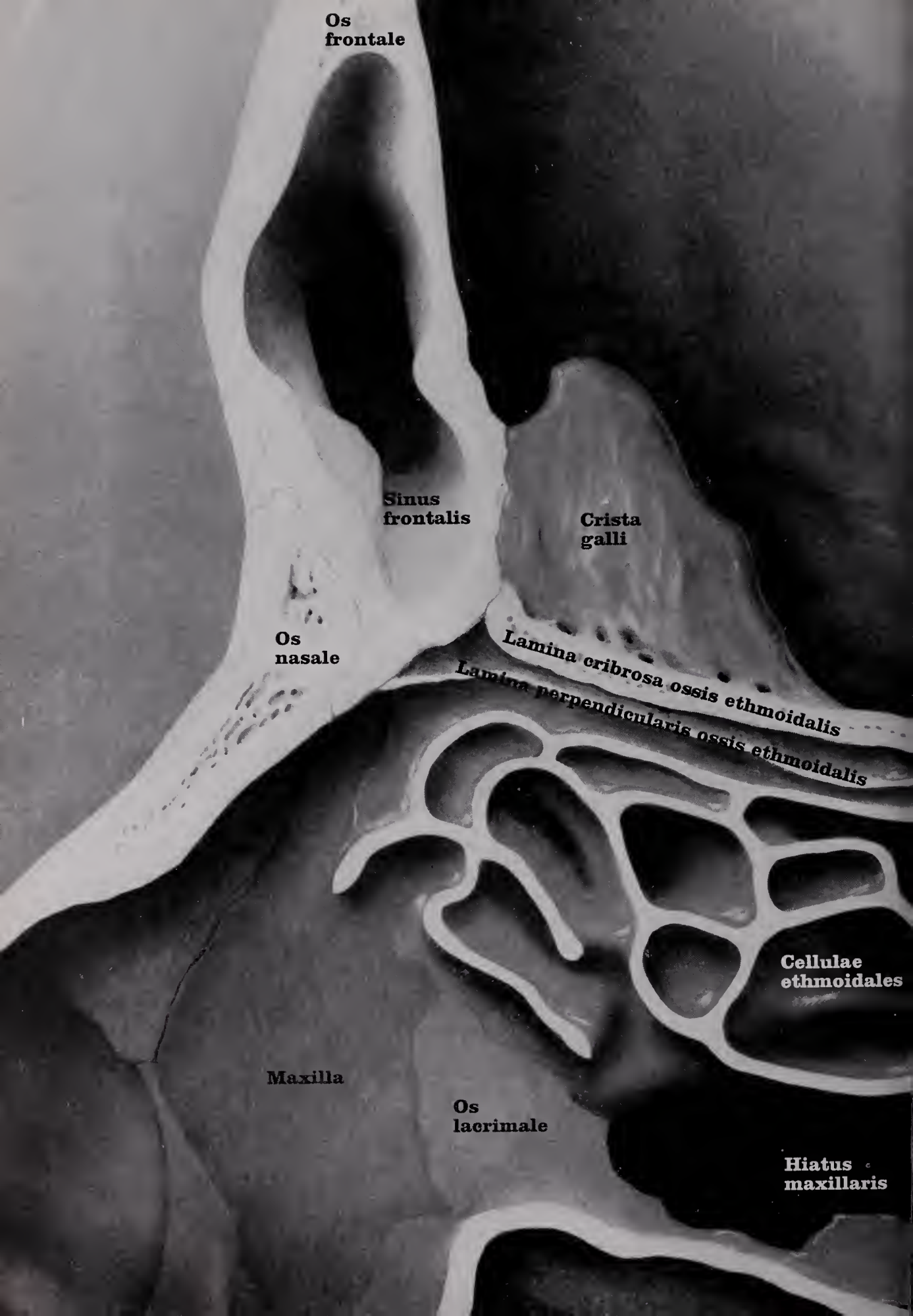
Lamina perpendicularis ossis ethmoidalis

**Cellulae
ethmoidales**

Maxilla

**Os
lacrimale**

**Hiatus
maxillaris**



special formula for a special problem

*specifically formulated
for symptomatic
relief of sinus headache*

Sinus headache is not a single entity, but a chain reaction of pain. It is facial pain—deep, dull, aching and nonpulsating. It is referred pain—originating in the nose and sinuses but felt at another site. It may become generalized pain and tension in head and neck. It is one or all of these.

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It provides two analgesics to relieve pain and discomfort...an effective oral decongestant to reduce mucosal congestion... and an antihistamine to help control allergic manifestations.

Side Effects: Epigastric distress, drowsiness, dizziness, insomnia and nervousness.

Precautions: Instruct patients not to drive or operate machinery if drowsiness occurs.

Use with caution in patients with thyroid disease, heart disease, hypertension, diabetes or kidney disease. Excessive dosage or prolonged use may cause kidney damage.

Dosage: Adults—2 tablets every 4 hours.

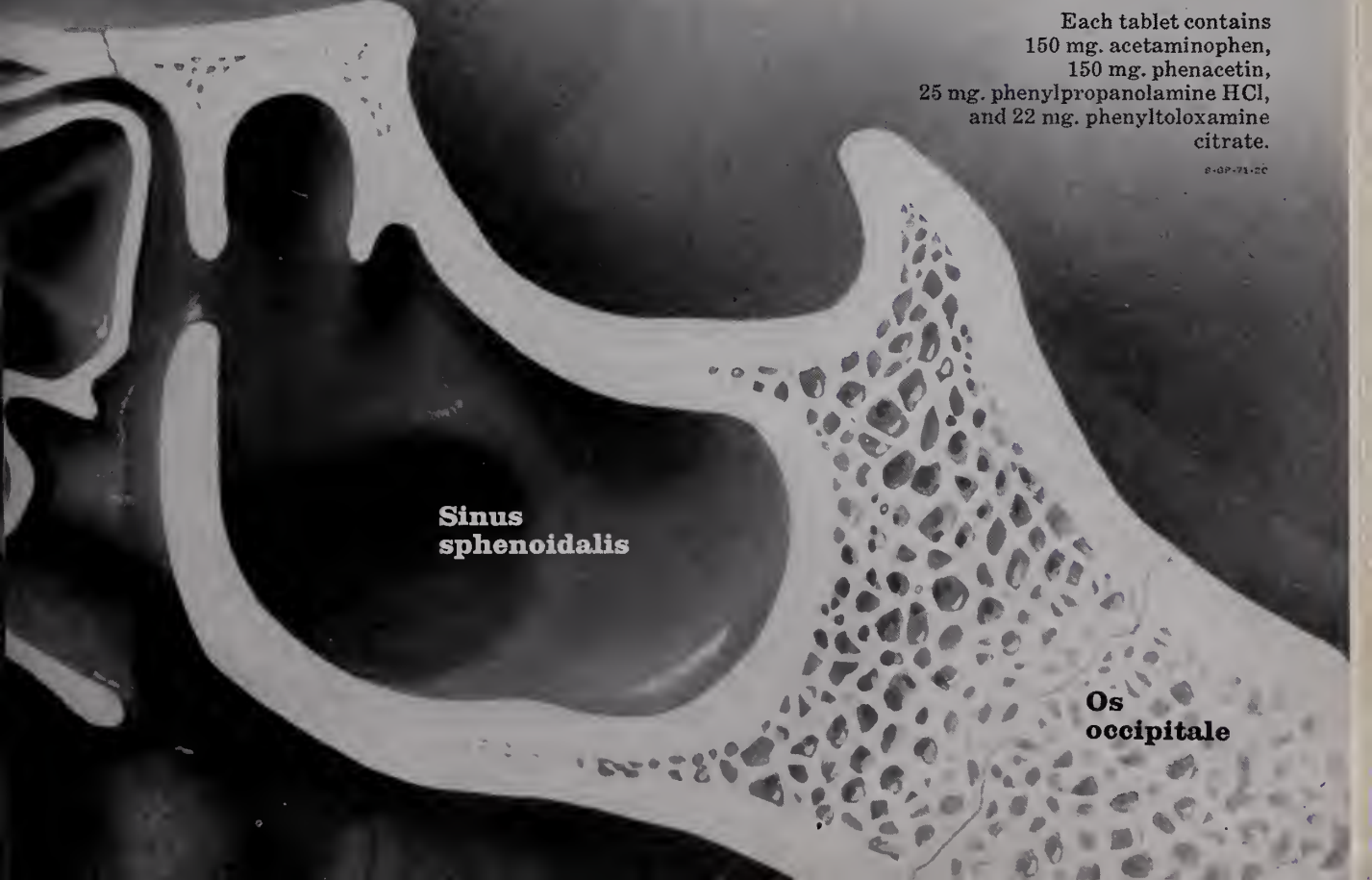
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150 mg. acetaminophen,
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and 22 mg. phenyltoloxamine
citrate.

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**Sinus
sphenoidalis**

**Os
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(norethindrone 2 mg. $\bar{c}$ mestranol 0.1 mg.)

for multiple contraceptive action that has produced a record of unexcelled effectiveness

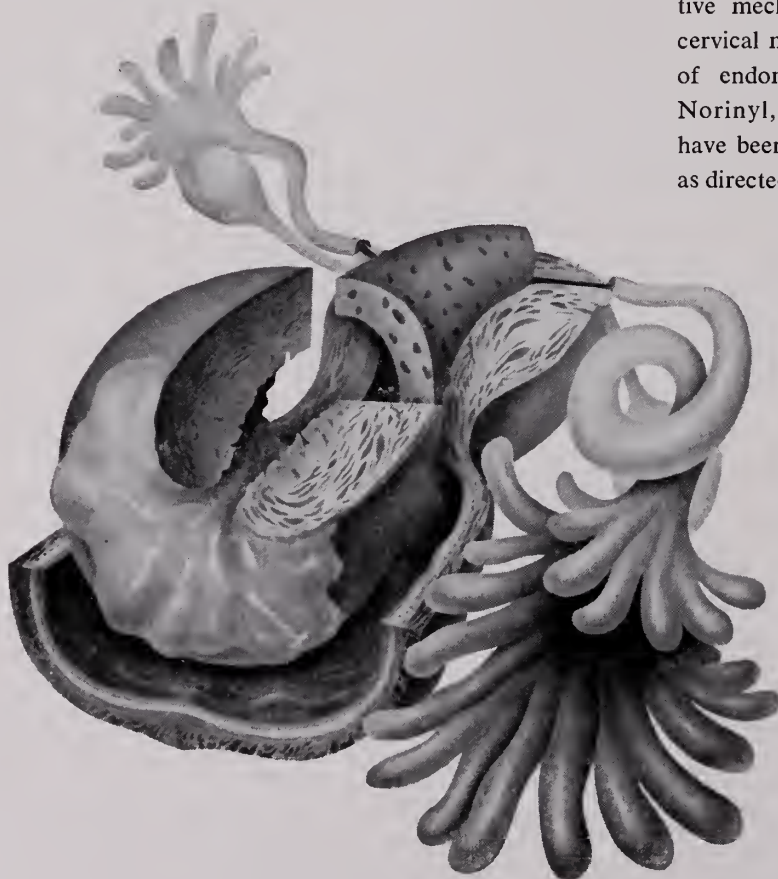
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2 time-proved hormonal agents**

**production of a cervical mucus hostile to
sperm motility and vitality**

**creation of an endometrium unreceptive
to egg implantation**

no unplanned pregnancies

Norinyl provides multiple action for maximum assurance of success. It does not depend on ovulation inhibition alone for contraceptive effectiveness. The mechanism of action of combined hormonal therapy results in ovulation inhibition reinforced by other protective mechanisms, including a hostile cervical mucus¹⁻¹³ and an acceleration of endometrial changes.^{1-3,7-16} With Norinyl, no unplanned pregnancies have been reported to date when used as directed.



plus important supportive benefits that help her through those critical early months of oral contraception

low incidence of side effects

Low incidence of BTB and spotting, nausea and amenorrhea tends to minimize side effect problems and increases patient cooperation.

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An unbreakable "confusionproof" package makes it easy to adhere to prescribed dosage schedule: individually sealed tablets numbered from 1 through 20 *plus* monthly calendar record enables patient to double-check dosage intake by day and corresponding tablet number.



Contraindications: Thrombophlebitis or pulmonary embolism (current or past). Existing evidence does not support a causal relationship between use of Norinyl and development of thromboembolism. While a study which was conducted does not resolve definitively the possible etiologic relationship between progestational agents and intravascular clotting, it tends to con-

firm the findings of the Ad Hoc Advisory Committee appointed by the Food and Drug Administration to review this possibility. Cardiac, renal or hepatic dysfunction. Carcinoma of the breast or genital tract. Patients with a history of psychic depression should be carefully studied and the drug discontinued if depression recurs to marked degree. Patients with a history of cerebral vascular accident.

Warning: Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn.

Precautions: By May 1963, experience with norethindrone 2 mg.—mestranol 0.1 mg. had extended over 24 months. Through miscalculation, omission or error in taking the recommended dosage of Norinyl, pregnancy may result. If regular menses fail to appear and treatment schedule has not been adhered to, or if patient misses two menstrual periods, possibility of pregnancy should be resolved before resuming Norinyl. If pregnancy is established, Norinyl should be discontinued during period of gestation since virilization of the female fetus has been reported with oral use of progestational agents or estrogen. When lactation is desired, withhold Norinyl until nursing needs are established. Existing uterine fibroids may increase in size. In metabolic or endocrine disorders, careful clinical preevaluation is indicated. A few patients without evidence of hyperthyroidism had elevated serum protein-bound iodine levels, which in the light of present knowledge, does not necessarily imply hyperthyroidism. Protein-bound iodine increased following estrogen administration. Bromsulphalein retention has occurred in up to 25% of patients without evidence of hepatic dysfunction. Studies from 24-hour urine collections have shown an increase in aldosterone and 17-

ketosteroids and decrease in 17-hydroxycorticoid levels. Thus, Norinyl should be discontinued prior to and during thyroid, liver or adrenal function tests. Because progestational agents may cause fluid retention, conditions such as epilepsy, migraine and asthma require careful observation. Thus far no deleterious effect on pituitary, ovarian or adrenal function has been noted; however, long-range possible effect on these and other organs must await more prolonged observation. Norinyl should be used with caution in patients with bone, renal or any disease involving calcium or phosphorus metabolism. Side Effects: Intermenstrual bleeding; amenorrhea; symptoms resembling early pregnancy, such as nausea, breast engorgement or enlargement, chloasma and minor degree of fluid retention (if these should occur and patient has not strictly adhered to medication plan, she should be tested for pregnancy); weight gain; subjective complaints such as headache, dizziness, nervousness, irritability; in a few patients libido was increased. In a total of 3,090 patients, 2.2% discontinued medication because of nausea.

NOTE: See sections on contraindications and precautions for possible side effects on other organ systems.

Dosage and Administration: One Norinyl tablet orally for 20 days, commencing on day 5 through and including day 24 of the menstrual cycle. (Day 1 is the first day of menstrual bleeding.)

Availability: Dispensers of 20 and 60 tablets; bottles of 100.

References: 1. Council on Drugs. JAMA 187:664 (Feb. 29) 1964. 2. Brvans, F. E.: Canad Med Ass J 92:287 (Feb. 6) 1965. 3. Goldzieher, J. W.: Med Clin N Amer 48:529 (Mar.) 1964. 4. Cohen, M. R.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965. 5. Hammond, D. O.: Ibid. 6. Rice-Wray, E., Goldzieher, J. W., and Aranda-Rosell, A.: Fertil Steril 14:402 (Jul.-Aug.) 1963. 7. Goldzieher, J. W., Moses, L. E., and Ellis, L. T.: JAMA 180:359 (May 5) 1962. 8. Kempers, R. D.: GP 29:88 (Jan.) 1964. 9. Tyler, E. T.: JAMA 187:562 (Feb. 22) 1964. 10. Rudel, H. W., Martinez-Manautou, J., and Maqueo-Topete, M.: Fertil Steril 16:158 (Mar.-Apr.) 1965. 11. Flowers, C. E., Jr.: N Carolina Med J 25:139 (Apr.) 1964. 12. Goldzieher, J. W.: Appl Ther 6:503 (June) 1964. 13. The Control of Fertility. Report adopted by the Committee on Human Reproduction of the American Medical Association. JAMA 194:462 (Oct. 25) 1965. 14. Flowers, C. E., Jr.: JAMA 188:1115 (June 29) 1964. 15. Merritt, R. I.: Appl Ther 6:427 (May) 1964. 16. Newland, D. O.: Paper presented at Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965. Reported in Med Sci 16:26 (Nov.) 1965.

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Special Article

Camping Opportunities

for
the
Child
With
Diabetes
Mellitus*

DONNELL D. ETZWILER, M.D.**
St. Louis Park, Minnesota

SEVERAL YEARS ago we published an article in this Journal describing the Minnesota State Camp for children with diabetes mellitus.¹ Since that time, significant changes and expansion in this program have taken place which should be of interest to physicians practicing in this area.

This is the tenth anniversary of Camp Needlepoint, which was conceived by Mr. Ronald Youngquist of St. Paul, Minnesota, and supported by the Twin Cities Diabetes Association. The size of the camp has increased from an initial 21 children in 1957 to 140 in 1966; unfortunately, again this year, the camp has had to turn away a significant number of children because of limited space. The camp utilizes the facilities of the St. Paul Y.M.C.A. Camp St. Croix, three miles south of Hudson, Wisconsin, overlooking the St. Croix River. Facilities here are rented for a one-week period the latter part of August each year.

The initial purpose of Camp Needlepoint was to provide camping opportunities for children with diabetes, since they are frequently unable to attend other camps. In 1960, however, it was decided the camp would serve two additional functions: (1) to further instruct these children and their parents in the proper care and management of diabetes mellitus; and (2) to permit the camp to serve as a resource tool and enable professional personnel to gain further insight into the nature of this disease process. Over the past few years it has become increasingly apparent that one of the greatest benefits derived from the camp is the opportunity for children with diabetes mellitus to meet and live with other campers with

*Supported by the St. Louis Park Medical Research Foundation.

**St. Louis Park Medical Center, Minneapolis, Minnesota.

One of the Contributing, Coordinating Editors of this special issue.

Requests for reprints should be addressed to the St. Louis Park Medical Center, 4959 Excelsior Blvd., Minneapolis, Minnesota.

Continued



Figure 1



Figure 2



Figure 3



Figure 4

the same disease. This experience has provided tremendous psychological benefit for these children.

In addition to the camping program at Camp Needlepoint, a wilderness camping program was introduced five years ago. This adventure sends groups of diabetic teen-aged boys, a physician and a guide into the wilderness areas for a seven-day canoeing experience.

Camping

Activities at Camp Needlepoint include all facilities, personnel, and programs utilized by Camp St. Croix during their regular summer program. Campers with diabetes are accepted from nine thru 16 years of age. Each cabin group consists of eight campers, the counselor and an assistant counselor. Most of the camp's male counselors and program directors are provided by Camp St. Croix; however, some of our past campers also serve in this capacity. Acquisition of good female counselors has been relatively easy; this job has appealed particularly to our past girl campers as well as student and graduate nurses. There are many applications for these jobs each summer with a high percentage of returnees year after year. The use of previous campers has many obvious advantages, and we have recently instituted an active counselor-in-training program, which has proven to be of more interest to teen-aged girls than boys.

The Indians

Cabin groupings are selected on the basis of age. The youngest campers, nine to 11 years old, are designated as "Indians," and this becomes the over-all theme of their camping program. These children are introduced to nature lore and crafts involving Indian projects. Evening council fires are held where Indian stories and dances are taught (Figure 1). All of the usual camping activities — swimming, hiking, cook-outs, boating, competitive sports, etc. — are also included in this program.

The Pioneers

Children 11 to 13 years of age are designated as "Pioneers" and their over-all

camping program is oriented accordingly. In addition to the usual activities, this group has cook-outs and overnight camping experiences (Figure 2).

*The Voyageurs**

The oldest group of campers, ages 13 to 16, are "Voyageurs," and they undertake three-day canoe trips, paddling 35 to 50 miles along the St. Croix River. A physician or graduate nurse accompanies each canoe group to assist and supervise diabetic care.

Camp begins on Sunday, and as the children arrive they are immediately registered and assigned to cabins. After an appropriate amount of time, their parents are asked to gather in the main lodge of the camp where the camping program is discussed with them by the Camp Director and the physician in charge. The parents are then acquainted with the camp routine and the nature of their child's diabetic management during his stay. It is also possible to review quickly some of the basic concepts of diabetic care with these parents at this time. The parents are also informed of past clinical studies that have been carried out at camp, and the project proposed for the current session is explained.

Medical Program

Our current medical program constitutes what we feel is ideal care for these children. Establishing a proper therapeutic regime serves not only to maintain these children in good control but also provides them with a rare learning experience. All children are encouraged to participate in a self-care program. Each child is provided with a kit which contains all materials necessary for urine testing and insulin administration. Campers are requested to bring their own syringes in order that they may become more familiar with this equipment. We do use plastic disposable insulin syringes on our overnight camp-outs and also on the canoe trips; these have proven to be very convenient. The schedule of the camp program is shown in Table 1.

The Morning Specimen

At 6:30 a.m. each camper arises and voids a first specimen which is discarded, and 15 to 20 minutes later a second sample of urine is obtained. It is this specimen that is tested, since it is felt that it more truly reflects the current level of glucose in the blood. This specimen is tested with the assistance of the cabin counselors if necessary; most children, however, are very adept at doing and reading urine tests. In the cabins for younger campers all results are checked by the counselor. Each camper then marks the results of his urine test on the record card which he keeps.

Insulin Requirement

As soon as this procedure is finished, the camp physician sits down with the camper and very quickly goes over the past urine records and, with the assistance of the camper, comes to a decision concerning the amount of insulin required. As soon as this is determined, the physician moves to the

TABLE 1

Daily Schedule	Camp Needlepoint
6:30	Reveille.
6:30-7:00	Urine testing.
7:00-8:00	Insulin administration.
8:00	Flag raising.
8:05	Breakfast.
8:45-9:30	Cabin clean-up.
9:30-12:00	Unit activities and program— craft, nature, athletics, hikes, etc.
10:00	Indian instructional swim.
10:45	Pioneer snack.
11:00	Pioneer swim.
	Indian snack.
12:00	Urine testing.
12:30	Dinner.
1:30-2:30	Rest hour and informal classes.
2:30-5:00	Unit activities and program.
2:30	Indian swim.
3:15	Pioneer snack.
3:30	Pioneer swim.
	Indian snack.
5:00	Urine testing.
5:30	Supper.
6:15	Challenge games.
7:15-7:45	Campfires by schedules as announced.
8:30	Urine testing and snacks.
9:30	Lights out.

Voyageur unit to set up swim and snack schedule with doctor's approval.

*See Test Your Word Score Page 363.

Continued

next camper. A registered nurse is then available to assist each camper in the preparation of his injection. For campers who routinely give their own insulin, the nurse merely checks the dosage, observes and reviews techniques. Campers who do not give their own injections but indicate some interest are taught by our nurses. We do not force campers to give their own injections; however, the social pressure in each cabin is sufficient in most cases to arouse these children's interest in self care (Figure 3). The opportunity to see and work with each camper individually each day has provided us with an excellent opportunity to teach on an effective and informed basis. The physician has a chance to explain why urine tests are important and how they relate to management. The possible effect of the day's planned activities are noted and a prophylactic approach to control is introduced.

The Difficult Diabetic

Urine tests are conducted four times each day — before each meal and at bedtime. Any child who has a 4+ test for sugar is required to test for acetone. Campers with acetone are requested to report to the infirmary where the physician appraises the situation. At bedtime all campers come to the dining room where the physician once again reviews each camper's record for the day and makes any necessary alterations in the evening snack. Midmorning and afternoon snacks are provided each day and may vary depending upon camp activities. After lunch each day the nurses, physicians, dietitians and camp director visit various cabin groups and spend 45 minutes to an hour in informal discussion of diabetes and its many aspects. In such a setting, group discussion has proved most beneficial and brings out many questions which would never be asked in a physician's office.

The Diet

All campers are placed on an exchange diet (Figure 4). At the time a camper's application is first submitted, the family is requested to send in the child's dietary prescription along with a list of the previous day's meals. These are then calculated and

compared. According to our head dietitian, Mrs. Rita Olson, this comparison reveals that less than 20% of the diet prescriptions are being followed at home. It is not infrequent that we receive dietary prescriptions that were given three to five years prior to the time these children attend camp. These are obviously inadequate and impossible to follow. Not all campers are familiar with the exchange dietary system when they first arrive at camp; however, it takes only one meal for them to comprehend the nature of the program. Dietary changes are permitted at the request of the camper. In general, we tend to increase all of our campers 200 calories above the diet given at home. This frequently has to be varied at camp, and on the canoe trips we have to increase the intake of calories from 500 to 2000 per day.

Research Activities

The gathering of such a large number of juvenile diabetics in one place at one time has provided an opportunity for us to carry out numerous clinical studies. Part of the lecture for parents on the first day is devoted to informing them of what the research activities will be and the results of previous programs. Rarely have we had a parent request that his child be excluded from these studies. The vast majority of the parents appreciate the work that is being done and realize that it is beneficial not only to their own child but to all other children with this condition. Some parents have even suggested that their non-diabetic children be used as controls.

What the Juvenile Diabetic Knows About His Disease²

The results of this study motivated us to determine what the families of these children knew about diabetes and how their environment might influence this condition. The following year biographic questionnaires were sent to all families, and we conducted a workshop for the parents, at which time tests on diabetes were given along with the Shipley-Hartford Retreat Scale to estimate IQs. The Minnesota Multiphasic Personality Inventory was sent to the parents, and additional questionnaires were sent to

the children's physicians and their school teachers.³

Glucagon in the Juvenile Diabetic

Camp has provided an excellent opportunity to assess the effect of glucagon in the juvenile diabetic; our studies revealed glucagon was highly effective in the juvenile diabetic experiencing hypoglycemia.⁴ Further studies at camp clarified some of the discrepancies appearing in the literature concerning the action of this hormone in juvenile diabetes.⁵

Urinary Tract Infection and Other Studies

The increased incidence of urinary tract infections among older diabetics has recently been disputed. Over a two-year period urine cultures were obtained from our campers, and the results indicated there was no increased frequency of urinary tract infections among these children.⁶ Other studies we have conducted dealt with determination of ocular pressure, blood pressures, funduscopic examinations and photographs, correlations of hypoglycemia and electroencephalographic changes, and comparisons of venous and arterial glucose levels. We feel that these efforts have been beneficial not only to our campers but to many other juvenile diabetics as well.

Psychological Experiences

The psychological value of camps for special illnesses, such as diabetes, is difficult to assess. From personal observation, I believe that most campers are much more willing to accept their disease after being at camp. The chance to work, play and live among others having the same condition is a rare opportunity for these children. In many instances it is the first time they have known other children with the disease, and they no longer feel quite so alone with their problem. At camp the disease is accepted as part of the daily routine and no sympathy is exhibited. They are expected to work, play and behave as any ordinary non-diabetic child would. Perhaps one of the best examples of the influence of group living is shown in an experience we had last summer. The first

morning of camp we found a group of nine-year-old girls gathered around one of their cabin mates who was administering insulin in her abdomen. Six of the eight campers in this cabin did not give their own insulin and seven of them had never seen it given in the abdomen. They were obviously interested in this technique and impressed that the girl was giving her own shot. The next morning all of these girls wanted to give their own insulin injections and insisted that it be given in their abdomens. This was done without any persuasion or suggestion from the staff. The medical staff is there to assist campers in procedures which the campers themselves decide upon.

Wilderness Camping

Our wilderness camping program was established five years ago in order to stimulate our older teenagers. These campers are 15 to 18 years of age and most have gone through our program at Camp Needlepoint. These trips have been either into the wilderness canoe areas in northern Minnesota or into the wilderness area along the Namakagon River in Wisconsin. Meals for these trips have been appropriately planned and all supplies and foods are carried in packs. These packs weigh between 75 and 85 pounds and the canoes weigh somewhere between 85 to 100 pounds. Each boy carries a pack or a canoe on portages. During the trip these boys paddle 200 to 250 miles in seven days (See photo on cover). One of the objectives of this program is to demonstrate to these boys and their families that diabetics who take care of themselves can be placed under rigorous conditions and do well. We have encountered no difficulties with this program; each group is accompanied by a physician and a trail guide.⁷

Conclusion

We believe that these camping programs are greatly beneficial to the young diabetic who so frequently has led a sheltered and extremely regulated life. Camp permits an opportunity to take part in vigorous outdoor living where good diabetic management is demonstrated and carried out, and its importance stressed.

References may be secured from the author.

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Contraindications: Contraindicated in individuals who have known hypersensitivity to any of its components. Not recommended for prophylaxis or in the management of infectious processes which may require more than 10 days of continuous therapy. If clinical judgement dictates therapy for longer periods, serial monitoring of liver function is recommended. Not recommended for subjects who have shown abnormal liver function tests, or hepatotoxic reactions to triacytyleandomycin.

Precautions and Adverse Reactions: *Triacytyleandomycin*, administered to adults in daily oral doses of 1.0 gm. for 10 or more days, may produce hepatic dysfunction and jaundice. Adults requiring 3 gm. of Signemycin initially should have liver function followed carefully and the dosage should be reduced as promptly as possible to the usual recommended range of 1.0 to 2.0 gm. per day. Present clinical experience indicates that the observed changes in liver

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Use with caution in lower than usual doses in cases with renal impairment to avoid accumulation of tetracycline and possible liver toxicity. If therapy is prolonged under such circumstances, tetracycline serum levels may be advisable. In long term therapy or with intensive treatment or in known or suspected renal dysfunction, periodic laboratory evaluation of the hematopoietic, renal and hepatic systems should be done. Formation of an apparently harmless calcium complex with tetracycline in any bone forming tissue may occur. Use of tetracycline during tooth development (3rd trimester of pregnancy, infancy and early childhood) may cause discoloration of the teeth. Reversible increased intracranial pressure due to an unknown mechanism has been observed occasionally in infants receiving tetracycline. Glossitis, stomatitis, proctitis, nausea, diarrhea, vaginitis and definite allergic reactions occur rarely. Severe anaphylactoid reactions have been reported as due to triacytyleandomycin. Photosensitivity and photoallergic reactions (due to the tetracycline) occur rarely. Medication should be discontinued when evidence of significant adverse side effects or reaction is present. Patients should be carefully observed for evidence of overgrowth of nonsusceptible organisms including fungi, which occurs occasionally, and which indicates this drug should be discontinued and appropriate therapy instituted. Steps should be taken to avoid masking syphilis when treating gonorrhea.



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Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonyleurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage. Make regular blood counts. Discontinue the drug and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The most common are nausea, edema and drug rash. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, or a generalized allergic reaction may occur and require withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

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TA-4919 PC

Sperling, I.L.: 3 Years' Experience
with Oxyphenbutazone in the
Treatment of Rheumatic Disorders,
Applied Therapeutics 6:117, 1964.

Watts, T.W., Jr.: Treatment of Rheu-
matoid Disorders with Oxyphenbu-
tazone, Clin. Med. 73:65, 1966.

76.9% of 407 patients

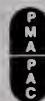
84.6% of 39 patients

New drugs take exams, too.

Today, virtually every medical school in the United States cooperates with pharmaceutical manufacturers in the clinical evaluation of new and promising drugs. Just as you might find it significantly more difficult to practice medicine without the useful new compounds made available through original pharmaceutical research in the past twenty years—prescription-drug manufacturers would find it equally difficult to obtain extensive, long-term, dependable evaluations of new therapeutic agents without the close cooperation of medical staffs and clinical

facilities of medical schools and teaching hospitals. Such cooperation leads toward more effective care of more patients—the common goal of medical and pharmaceutical research—toward reduction in the cost of disease, toward increase in useful longevity.

This message is brought to you as a courtesy of this publication on behalf of the producers of prescription drugs.



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Manufacturers Association
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Meetings and Announcements

You may fail to shine in the opinion of others, both in your conversation and actions, from being superior, as well as inferior, to them. — Greville

MARCH

Northwestern Pediatric Society — March-Spring meeting to be set.

Zumbro Valley Medical Society — March 1, Mann Hall, Rochester, 8:00 p.m.

Southwestern Minnesota Medical Society — March 6, Worthington, 7:00 p.m.

Hennepin County Medical Society and Hennepin County Academy of General Practice — March 6, Pick-Nicollet Hotel, Minneapolis, 6:00 p.m.

Scott-Carver County Medical Society — March 7,

Minnesota Academy of Medicine — March 8, Town & Country Club, St. Paul, 6:30 p.m.

St. Louis County Medical Society — March 9, Ex. Comm. at 6:00 p.m., regular meeting at 8:00 p.m., St. Mary's Hospital, Duluth.

Camp Release District Medical Society — March 10, Hunt Hotel, Montevideo.

Blue Earth Valley Medical Society — March 15, Interlaken Golf Club, Fairmont.

Twin City Urological Society — March 17, 6:00 p.m.

Hennepin County Academy of General Practice — March 20, Athletic Club, Minneapolis, 6:00 p.m.

Ramsey County Medical Society — 8:00 p.m. — March 27, 15th floor, Lowry Medical Arts Bldg., St. Paul.

Range Medical Society — March 28, Ex. & General Mtg., dinner at 7:00 p.m., Hibbing.

Area Health Careers Conference for junior, senior high school and college students, El Paso, March 3. Contact: Frank I. Gary, El Paso Public Schools, 1000 West Rio Grande Avenue, El Paso, Texas.

Symposium on "Immunologic Approaches to Mechanisms of Cutaneous Disease," New York University Medical Center, March 29-31. Contact: Office of the Recorder, New York Post-Graduate Medical School, New York, New York.

APRIL

National Methodist Convocation on Medicine and

Theology, April 5, 6, 7, in Rochester, Minnesota. Contact: National Methodist Convocation, P.O. Box 102, Rochester, Minnesota 55901.

Department of Pediatrics at the University of Wisconsin Medical Center, Madison, Wisconsin, will sponsor a three day Postgraduate Conference on "The Mentally Retarded Child," April 6, 7, 8. Contact: Harry A. Waisman, M.D., Joseph P. Kennedy Jr. Laboratory, University of Wisconsin Medical Center, Madison, Wisconsin 53706.

1967 American Industrial Health Conference, April 12-13, New York City, Americana Hotel. Contact: American Industrial Health Conference, 55 E. Washington St., Chicago.

11th Annual Post Graduate Course in Fractures and Trauma, April 19-22, Chicago, John B. Murphy Auditorium at 50 E. Erie Street. Tuition is \$80.00. Contact: James P. Ahstrom, Jr., M.D. Chairman, 55 East Erie Street, Chicago.

Department of Otolaryngology of the Illinois Eye and Ear Infirmary and the College of Medicine of the University of Illinois at the Medical Center, Chicago, will conduct a post graduate course in Laryngology and Bronchoesophagology, April 10-22, at the new Illinois Eye and Ear Infirmary, 1855 West Taylor Street, Chicago. Contact: University of Illinois Medical Center, P.O. Box 6998, Chicago.

18th Hahnemann Symposium: Epithelial-Mesenchymal Interactions, April 17-19, Sheraton Hotel, Philadelphia. Sponsored by the Hahnemann Medical College and Hospital in Philadelphia. Contact: Raul Fleischmajer, M.D.

JUNE

A continuation course in Clinical Electroencephalography, June 5-7, Philadelphia, Pa. Sponsored by the American EEG Society and is designed for physicians who have had little or no formal EEG training. Inquiries address to: Donald W. Klass, EEG Course Director, Mayo Clinic, Rochester, Minnesota.

How Much Life Insurance?

VERY FREQUENTLY we are confronted with this question from a client: "How much life insurance should I have?" The client expects an answer in terms of "averages" or some "rule of thumb." True, there are many such "averages" and "rules of thumb" in existence today. Some say that a person should spend approximately 10% of his annual income for insurance. How much insurance will this buy? We all know that \$1,000 may pay the annual premium on a \$15,000 Retirement Income policy, or it may pay the annual premium on \$170,000 of Decreasing Term insurance. The age of the insured and the type of insurance are the deciding factors. Another fallacy in this approach is the assumption that everyone can afford 10% of his annual income for insurance — no more — no less. Obviously, this point needs no explanation; it just isn't true.

A second approach is to try to fix the dollar amount of insurance according to income. Some advocate four to five times annual income. There are many pitfalls in this approach. To use an exaggerated example, this approach would dictate \$300,000 insurance for a doctor, age 55, with single net income \$75,000 and assets of \$450,000. At the other extreme, it would dictate \$80,000 insurance coverage for the 33-year-old doctor earning \$20,000, with a 30-year-old wife and four young children, \$25,000 in debt and with no income-producing assets. In neither case would the doctor have the proper amount of insurance in his portfolio.

What, then, is the answer to the question, "How much life insurance?" In our opinion, there can be no stock answer and no application of "guides" or "rules of thumb." Every such question must be approached from an individual standpoint and answered after a thorough analysis of needs, present insurance, other assets, and finally, the client's ability

to pay the premium load required for such a program.

To approach an individual and personal problem on the basis of the "average" is like the man with his head in the oven and his feet in the freezer — *on the average* he feels just right. Such an approach to our clients' insurance problems would mean that only a scattered handful would have a *right* amount to afford the desired protection; but they all would have an *average* amount.

The following are some basic concepts that we advocate in planning an insurance program:

1. Using a realistic approach and realizing that insurance is a disaster-type protection, write down exactly what you want to provide for your family if you die. How much for debt, education, estate costs, current expenses and monthly income.

2. What will your present resources, including present insurance and all other assets, do toward fulfilling these needs?

3. What insurance is required to satisfy the remainder of your needs? In answering this, your insurance advisor will fill temporary needs with some of the various term contracts available. Permanent needs will probably best be satisfied with a low-cost permanent contract.

4. Finally, is the cost of the additional insurance reasonable and within your budget? If not, needs must be trimmed and/or more term insurance used.

By following this approach, we are not considering our client as an "average" or a "statistic;" we are considering him an individual. In summary, to assure an adequate life insurance program at a realistic cost, use an impartial adviser, take an individual approach, be realistic in weighing your needs and, finally, buy insurance for *protection*, not for investment purposes.

William D. Huntington*
Minneapolis, Minnesota

*Northern Division Manager, Professional Management Midwest.

The Stature of Mediocre Men

What makes a nation great is not primarily its great men, but the stature of its innumerable mediocre ones. — Ortega Y Gasset

MINNESOTA MEDICINE Cover Photographs

In order to encourage more physicians to submit color slides for use on the cover of MINNESOTA MEDICINE the competition is being discontinued. The picture editor now invites all physician-photographers to send 35 mm. color slides of suitable subjects for consideration as cover pictures. The format must be horizontal because of printing limitations. Pictures highlighting Minnesota seasons, places, and activities will have an automatic advantage. No limit as to the number of slides sent will be set, but all slides should be individually identified. All slides will be returned. Physicians whose pictures are used as covers will be recognized in MINNESOTA MEDICINE. We can use many more pictures than we have received in the past.

Men love to wonder, and that is the seed of our science. — Emerson



Physician's Diary

Intellect marches, but imagination rambles. — Comtesse Diane

Dr. Melvin Sinykin of Minneapolis was elected president of the Minnesota Obstetrical and Gynecological Society. Other officers are: **Dr. Grant Hartnagel**, Red Wing, vice president; **Dr. Peter J. Bartzen**, Duluth, assistant secretary-treasurer, and **Dr. Herschel B. Cope**, Virginia, board member.

* * *

Dr. John T. Kelly was re-elected chief of staff for 1967 of St. Mary's Hospital Medical Staff. **Dr. Berton D. Mitchell** was re-elected vice president and **Dr. Norman F. Stone** was re-elected secretary.

* * *

Doctors **David C. Dahlin** and **Mark B. Coventry** of the Mayo Clinic, Rochester, presented papers in the Scientific Program of the 34th Annual Meeting of the American Academy of Orthopaedic Surgeons in San Francisco in January.

* * *

Dr. N. L. Gault, Jr., associate professor of medicine and associate dean of the University of Minnesota's College of Medical Sciences, participated in the Third World Conference on Medical Education in New Delhi, India.

* * *

Dr. George B. Logan, professor of pediatrics, Mayo Clinic, Rochester, was named vice-president and president-elect of the American Academy of Pediatrics at the Academy's annual meeting.

* * *

Dr. O. Theron Clagett, head of a section of surgery in the Mayo Clinic, Rochester, and professor of surgery in the Mayo Graduate School of Medicine, was elected president of the Western Surgical Association at the annual meeting of the organization in Phoenix.

* * *

NEW LOCATIONS: **Dr. David B. Eaton** joined the staff of the Worthington Clinic. **Dr. Eaton** was formerly on the staff of the University of Iowa Medical School . . . **Dr. Matthew B. Smorstok** of Monticello has joined the staff of the University of Minnesota Health Service in Minneapolis . . . **Dr. Keith D. Larson**, a former Mayo Graduate School

resident in medicine, has been appointed medical director of the Moose Lake State Hospital . . . **Dr. Emmanuel Balcos** of Minneapolis will open up a practice in Morgan in July . . . **Dr. Curtis A. Johnson** is practicing in Waseca . . . **Dr. John Fluegel** has left the Olmsted Medical Group in Rochester to enter specialty training.

* * *

Dr. L. Emmerson Ward, a consultant in medicine of the Mayo Clinic, has been elected to his fourth term as chairman of the Mayo Clinic Board of Governors.

* * *

Dr. Robert A. Good, professor of pediatrics and microbiology at the University of Minnesota Medical School, delivered the annual Louis A. Greensfelder lecture at the Michael Reese Hospital and Medical Center, Chicago, in February. **Dr. Good** spoke on "Development and Involution of the Lymphoid Tissue in Relation to Immunologic Capacity."

* * *

Dr. Marvin M. D. Williams, consultant in biophysics in the Mayo Clinic, Rochester, and professor of biophysics in the Mayo Graduate School of Medicine, was elected vice president of the Radiological Society of North America, Inc., at the annual meeting of the organization at Chicago.

* * *

Dr. Clifford Stadem of Twin Valley was elected president of the Red River Valley Medical Society. Other officers elected were: **Dr. Earl Dagg** of Thief River Falls, vice president, and **Dr. H. D. Clapp** of Crookston, secretary-treasurer.

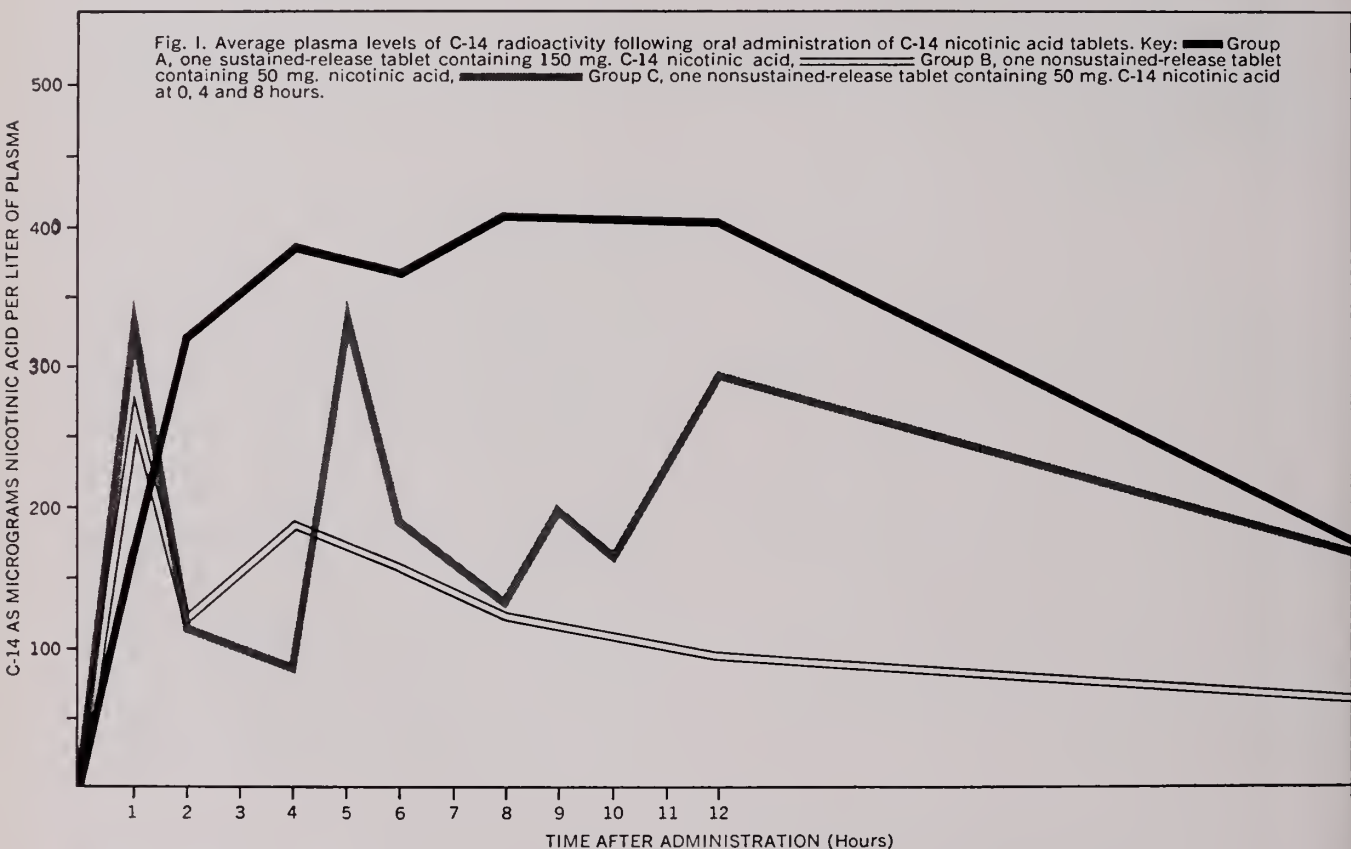
* * *

Dr. Bruce Douglass has been named president of the Minnesota Academy of Occupational Medicine and Surgery.

* * *

David R. Preston, assistant administrator of St. Mary's Hospital in Duluth, has been named associate director of the University of Minnesota Hospitals, and **John H. Westerman**, associate director of the University of Minnesota Hospitals, became director of the Hospitals in January.

Sustained circulatory, respiratory and cerebral stimulation for the



(fewer absent doses by
absent-minded patients)

Human volunteer subjects were administered Geroniazol TT tablets with the nicotinic acid component made radioactive with C-14. Plasma and urine samples were analyzed. (See Figures I and II) The radioactive tracer study substantiated the previous clinical evidence that the release of nicotinic acid from the Geroniazol TT tablet produced a gradual rise in plasma levels to a plateau for a total of 12 hours and more.

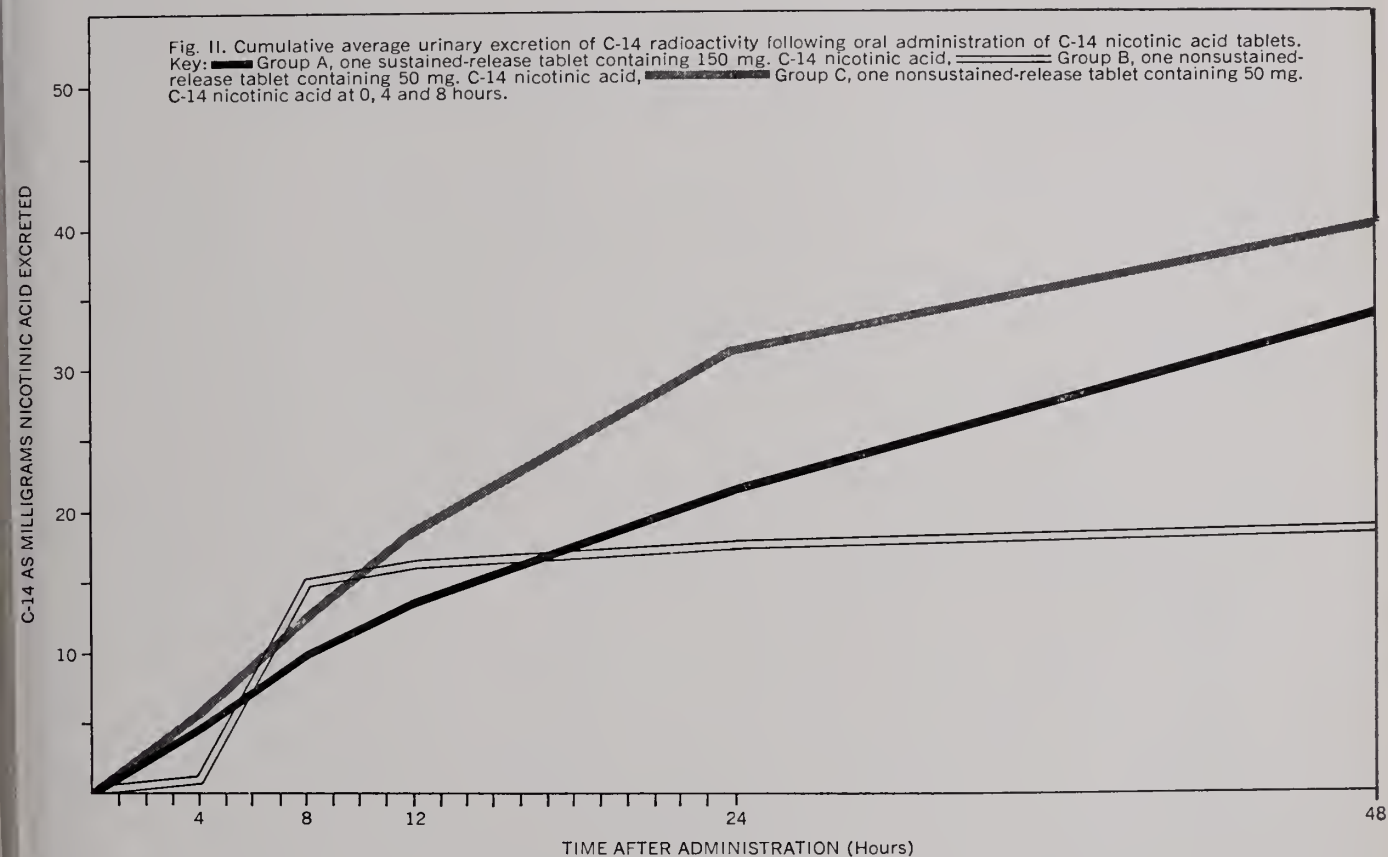
Such proven sustained activity makes the management of geriatric patients much easier by minimizing the possibility of neglected doses through absent-

mindedness or senile confusion. Therapy *can* be continuous on a daily dose of only one Geroniazol TT tablet every 12 hours.

The gradual release of nicotinic acid in Geroniazol TT will provide the well-known peripheral vasodilation needed in patients with deficient circulation and with a minimum amount (if any) of "flushing." Also, cerebrovascular circulation is complemented by pentylentetrazol, long-established as a cerebral and respiratory stimulant.

Geroniazol TT improves the typical, unfortunate, signs of senile confusion. Patients become more alert,

ged and debilitated



less confused and moody. Personal care, memory, emotional stability, social attention improve. Fatigue, apathy and irritability are reduced.

A prescription for 100 tablets of Geroniazol TT will permit your patients to enjoy the benefits of time-prolonged nicotinic acid/pentylenetetrazol therapy, at an economical price. Dosage is only one tablet every 12 hours.

Contraindications: There are no known contraindications.

Precautions: Exercise caution when treating patients with a low convulsive threshold.

Side Effects: Side effects are rarely encountered, however due to the vasodilatation effect of nicotinic acid, transitory mild nausea, flushing, tingling and pruritus are possible.

Dosage: One tablet every 12 hours.

Supplied: Prescribe bottles of 100 tablets, to take advantage of recent price reduction.

References: 1. Report by Nuclear Science & Engineering Corp., Pittsburgh, Pa., in files of Philips Roxane Laboratories. 2. Connolly, R.: W. Virginia Med. J. 56:263 (Aug.) 1960. 3. Curran, T. R., and Phelps, D. K.: Am. Pract. & Digest Treat. 11:617 (July) 1960.



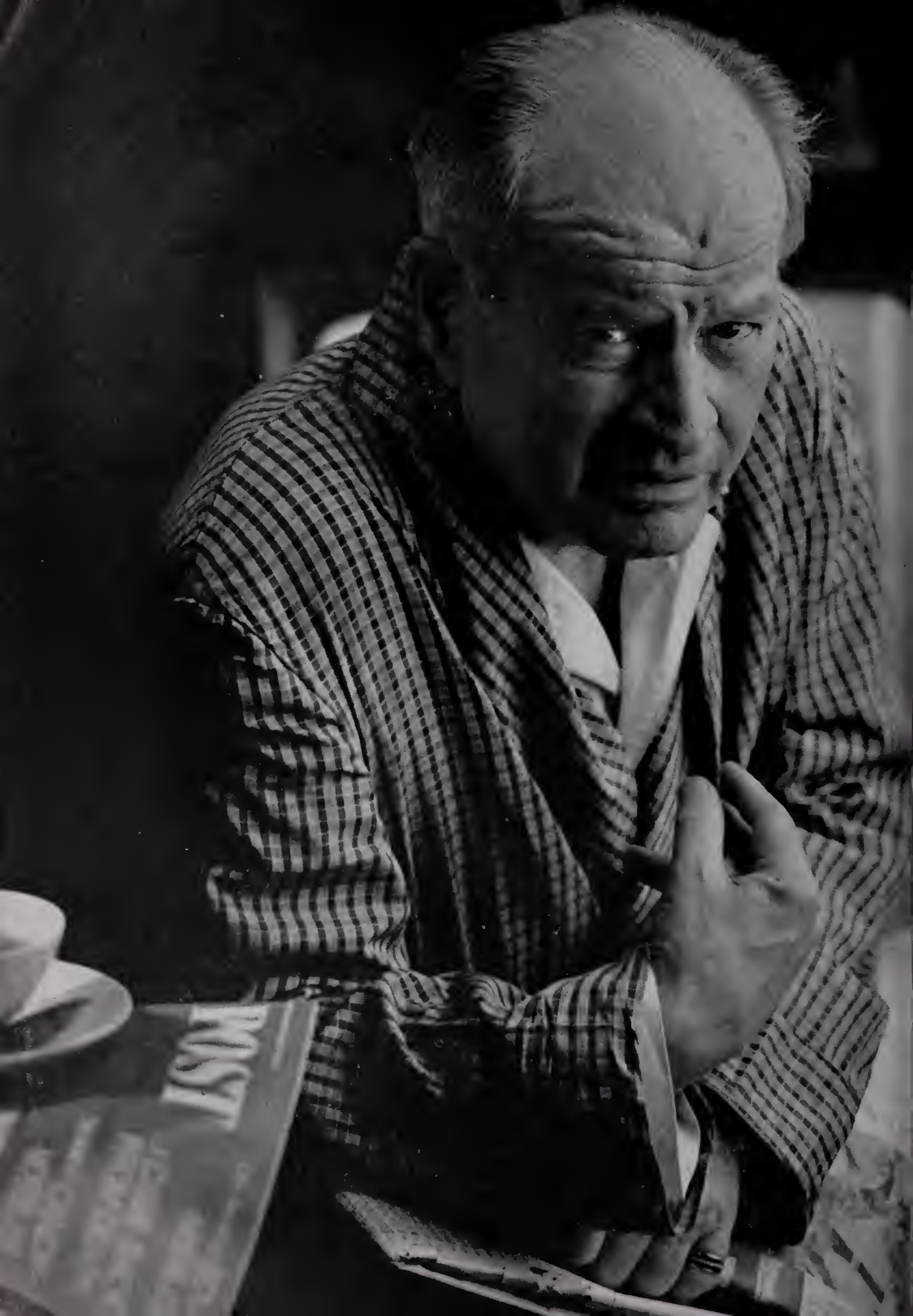
"First with the Retro-Steroids"

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Division of Philips Roxane, Inc., Columbus, Ohio
A Subsidiary of Philips Electronics and
Pharmaceutical Industries Corp.

Geroniazol[®] TT

nicotinic acid 150 mg., pentylenetetrazol 300 mg.
Tempotrol[®] Time Controlled Tablet



I'm supposed to get up and do things?

With my heart?

It's entirely natural—and may even be desirable—for the cardiovascular patient to be somewhat anxious about himself.

But when anxiety leads to unreasonable self-imposed limitations and restrictions . . . when it aggravates cardiovascular symptoms . . . when it interferes with restful sleep, measures to help alleviate the anxiety are probably in order.

One measure, of course, is reassurance. Another, adjunctive measure, is EQUANIL (meprobamate).

Over a decade of experience has shown that EQUANIL (meprobamate) is generally well tolerated as well as effective. Side effects are usually limited to transient drowsiness; serious, therapy-interrupting side effects are rare.

Cautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use may result in dependence or habituation in susceptible persons—as ex-addicts, alcoholics, severe psychoneurotics. After prolonged high dosage, drug should be withdrawn gradually to avoid possibly severe withdrawal reactions including epileptiform seizures. Side effects include drowsiness and, rarely, allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute non-thrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. Meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Warn patients of possible reduced alcohol tolerance. Should drowsiness, ataxia, or visual disturbances occur, dose

should be reduced. If symptoms persist, patients should not operate vehicles or dangerous machinery. A few cases of leukopenia, usually transient, have been reported following prolonged dosage. Other blood dyscrasias—aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia—have occurred rarely, almost always in the presence of known toxic agents. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. Prescribe very cautiously for patients with suicidal tendencies. Suicidal attempts should be treated with immediate gastric lavage and appropriate supportive therapy.

Contraindications: History of sensitivity to meprobamate.

Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

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A quality controlled product of
Wyeth Laboratories Philadelphia, Pa.

to help relieve anxiety and tension occurring
alone or secondary to organic disease

Equanil[®]
(meprobamate)



**How long will it take him
to recover from the flu
if he just doesn't care?**



Does he really care?
Is he alert, encouraged,
positive and optimistic
about getting out of bed
and back to work soon?

Or is he giving in to
the depressing impact
of confinement?

When functional fatigue
complicates convalescence,
Alertonic can help...

Pleasant-tasting Alertonic is pipradrol hydrochloride—an effective cerebral stimulant whose gentle analeptic action helps counteract the apathy and inertia that so often delay convalescence—together with an excellent vitamin and mineral formula, in a satisfying 15% alcohol vehicle.

Nothing fosters confidence and a sense of well-being better than your own personal warmth, understanding and encouragement together with Alertonic to help insure prompt response.

Adequate dosage is important: Prescribe Alertonic—one tablespoonful t.i.d., 30 minutes before meals...tastes best chilled.

And for your patient's sake, prescribe Alertonic in the convenient, economical one-pint bottle.

Alertonic[®]

Available Only On Prescription

Each 45 cc. (3 tablespoonfuls) contains: alcohol, 15%; pipradrol hydrochloride, 2 mg.; thiamine hydrochloride (vitamin B₁) (10 MDR*), 10 mg.; riboflavin (vitamin B₂) (4 MDR), 5 mg.; pyridoxine hydrochloride (vitamin B₆), 1 mg.; niacinamide (5 MDR), 50 mg.; choline,† 100 mg.; inositol,† 100 mg.; calcium glycerophosphate, 100 mg. (supplies 2% MDR for calcium and for phosphorus) and 1 mg. each of the following: cobalt (as chloride), manganese (as sulfate), magnesium (as acetate), zinc (as acetate), and molybdenum (as ammonium molybdate).

*Multiple of adult Minimum Daily Requirement supplied.

†The need for these substances in human nutrition has not been established.

Indications: 1. Functional fatigue such as that often associated with: a depressing life experience or stressful time of life; advancing years; convalescence; limited activity or confinement. 2. Poor appetite and vitamin-mineral deficiency as they occur in: patients having faulty eating habits; geriatric patients who are losing interest in food; patients convalescing from debilitating illness or surgery.

Contraindications: As with other drugs with CNS stimulating action, Alertonic is contraindicated in hyperactive, agitated or severely anxious patients and in chorea or obsessive compulsive states.

Side effects: Reports of overstimulation have been rare. Patients who are known to be unduly sensitive to the effects of stimulant drugs should be observed carefully in the initial stages of treatment.

Dosage: Adults, 1 tablespoonful; children (over 15 years old), 1 to 2 teaspoonfuls; children (4 to 15 years old), 1 teaspoonful. To be taken three times daily 30 minutes before meals.

Merrell

THE WM. S. MERRELL COMPANY
Division of Richardson-Merrell Inc.
Cincinnati, Ohio 45215

6-7907



"George wants to know if it's okay to take his cold medicine now, Doctor, instead of seven o'clock?"



The long-continued action of Novahistine LP should help you both get a good night's sleep. Two tablets in the morning and two in the evening will usually provide round-the-clock relief by helping clear congested air passages for freer breathing. Novahistine LP also helps restore normal mucus secretion and ciliary activity—normal physiologic defenses against infection of the respiratory tract. Use cautiously in individuals with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Caution ambulatory patients that drowsiness may result. Each Novahistine LP tablet contains: phenylephrine hydrochloride, 25 mg., and chlorpheniramine maleate, 4 mg.

NOVAHISTINE[®] LP



PITMAN-MOORE Division of The Dow Chemical Company, Indianapolis



AMA 116th Annual Convention • Atlantic City, New Jersey • June 18-22, 1967

Come to Atlantic City—one of America's favorite by-the-sea playgrounds—and join your colleagues at the AMA's 116th ANNUAL CONVENTION!

Fine hotels and motels, excellent restaurants, plus all the advantages of a lively resort make this year's Convention a must for you and your family. Atlantic City provides a superb setting for a summer classroom and all the latest techniques of modern medicine. Plan to be one of the participants in this rewarding four day postgraduate education program.

• Four general scientific sessions • 23 section programs • 575 scientific and industrial exhibits. Lectures, panel discussions, motion pictures, and color television. Plan to attend—continue your postgraduate education.

RESERVE NOW for the **SCIENTIFIC AWARDS DINNER** in honor of the Scientific Award Winners—Wednesday, June 21, 1967. Since space is limited, we suggest you make your reservations before June 1, 1967. Tickets are \$10.00 each, payable in advance.

See JAMA May 8, 1967 for complete scientific program—forms for advance registration and hotel accommodations.

Classified

Classified advertising rates are twenty (20) cents a word; minimum monthly charge \$5.00; key number, fifty (50) cents additional.

Replies to advertisements with key numbers should be mailed in care of MINNESOTA MEDICINE, 496 Lowry Medical Arts Bldg., St. Paul, Minn. 55102

INTERNIST AND GENERAL PRACTITIONER wanted to join a four-man clinic group in suburban Minneapolis. Laboratory and X-ray with part-time radiologist. Excellent open hospital staff association. Salary to start with early partnership. Write: MINNESOTA MEDICINE — 372; 496 Lowry Medical Arts Bldg., St. Paul 55102.

WANTED: young internist and pediatrician, board certified or eligible, to join five-man group consisting of three GPs, a general surgeon and a radiologist. College town serving population of 22,000 thirty miles from Twin Cities. Salary open with early partnership opportunity. Write or call collect: Ed Jenkins, Manager, River Falls Medical Clinic, River Falls, Wisc. Phone 425-5322.

DON'T OVERLOOK THIS . . . 3 months' rent free in modern medical clinic — successful location in N.W. suburb of Minneapolis. Come see anytime — 36th and Noble Avenue North. Noble Drug, Ju 8-9449, Ben or Lou.

FOR RENT: Space available for surgical subspecialists. Excellent location. Near Unity Hospital, 10 minutes from Mercy. Share space with General & Thoracic Surgeon and 2 interns. Call Mrs. Winkel — 560-1700, Fridley.

FOR LEASE IN TWIN CITIES — small clinic, large parking area. With lease goes incredibly lucrative general practice, patients' records and excellent staff, at NO FEE. Write: MINNESOTA MEDICINE — 371; 496 Lowry Medical Arts Building, St. Paul 55102.

RESIDENCIES IN PHYSICAL MEDICINE and Rehabilitation offer challenge and opportunity in a growing field. Comprehensive training utilizing Mayo Clinic facilities and faculty, at \$3600 to \$10,000 stipend. Attractive community, excellent school system, cultural advantages. Contact Gordon Martin, M.D., Mayo Graduate School of Medicine, Rochester, 55901.

WANTED: Young general practitioner to join five-man group consisting of three GPs, a general surgeon, and radiologist. College town serving population of 22,000 30 miles from Twin Cities. Also need LOCUM TENENS in general practice. Contact: Ed Jenkins, Manager, River Falls Medical Clinic, River Falls, Wisconsin, Phone 425-5322.

GENERAL PRACTITIONER wanted to join well-established practitioner. New clinic building — 90 miles east of St. Paul — city of 14,000. Early partnership with full hospital facilities. Ideal location. L. W. Picotte, M.D.; Chippewa Falls, Wisconsin.

FOR SALE: Mattern x-ray unit K.V.-60. Good for chest and extremity work. Also an examining table, instrument cabinet, E.K.G., and other equipment.

Contact L. A. Whitesell, Jr., M.D. 207 South 1st Street, Buffalo, Minnesota 55313.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 289; 496 Lowry Medical Arts Building; St. Paul, 55102.

OFFICE SPACE now available in busy Bloomington. 713 square feet of new space in building with busy group of G.P.'s, dentist and suburban OB-GYN office. Ideal for ophthalmology, ENT or pediatrics. 8040 Penn Avenue South. 888-9211.

WANTED — Internist, board certified or qualified, to associate with two board certified internists. Ten man multi-specialty group. (Lenont Peterson Clinic, Virginia, Minnesota) — Heart of the expanding taconite industry.

GENERAL PRACTITIONER, associate, urgently needed. Unopposed practice established 20 years. 32 bed new hospital with additional 20 bed chronic unit. Good anesthesia coverage, lab. facilities. Excellent clinic one block from hospital. Salary with early partnership. Locum tenens also considered. Call collect 218-782-4725 or write Klefstad Clinic, Greenbush, Minnesota.

WANTED: GP to join clinic serving population area of 12,000. City has new hospital, new clinic building, two nursing homes, new Jr-Sr high school, new swimming pool, rich farming area in Red River Valley. Fishing and hunting nearby; metropolitan city close by. Salary open and partnership if interested. Write or call Warren Clinic, Warren, Minnesota 742-6231, area code 218.

THREE MAN group in North West Wisconsin Resort, State Conservation and Retirement Area needs two more physicians adequately to serve their practice. Facilities offered are three-room physician suites, X-ray and lab under AMT technician, RN-only nursing personnel. New accredited thirty-two bed hospital and forty-six bed nursing home. Deer and duck hunting, fishing within five minutes of town. Internist most needed; generalists welcomed. Will meet any reasonable salary request. Partnership after one year. Write: MINNESOTA MEDICINE — 365; 496 Lowry Medical Arts Building, St. Paul 55102.

GENERAL PRACTITIONER — to join established five-man group consisting of three general practitioners, a general surgeon, and an internist. Excellent clinic facilities situated adjacent to the city hospital. Starting salary negotiable. Retirement plan and many other fringe benefits. Call or write: Richard F. Lehigh, Owatonna Clinic, Owatonna, Minnesota 55060. Phone: 451-1120.

CLASSIFIED ADVERTISEMENTS

EXCELLENT OPPORTUNITY for Intern or Resident finishing in June or July to try practice in specialty group on locum tenens basis — June 1 thru August 31, 1967. Replacing Internist on leave of absence. Option of remaining on staff if desired. Salary open. Write or call collect, 281-3184, Northwestern Clinic, Crookston, Minnesota.

GENERAL PRACTITIONER wanted by two-man general practice group. Surgery within capability. Community Hospital. Eligible partnership if preferred. Write: MINNESOTA MEDICINE — 393, 496 Lowry Medical Arts Building, St. Paul — 55102.

RESIDENTS IN PSYCHIATRY — Opening for July 1, 1967. Stipend \$11,400 for physicians just completing internship. Federal stipend of \$12,000 annually with an extra \$3600 tax exemption available to physicians with 4 years non-psychiatric training or experience following internship. Graduates of American schools must be eligible for Iowa licensure. Foreign graduates must have ECFMG certificate. This is an acute treatment hospital with 450 in-patients and large outpatient department, children's unit under direction of Board-certified Child Psychiatrist. Intensive didactic teaching program with rich clinical experience directed toward preparing the resident for Board certification. Thirteen senior staff members including ten Board certified. Numerous consultants authorized for 18 residents. Affiliation with University of Iowa. Enthusiastic training and treatment programs that are best appreciated by a personal visit. Write W. C. Brinegar, M.D., Superintendent or John J. Worthington, M.D., Director of Psychiatric Training, Mental Health Institute, Cherokee, Iowa 51012.

GENERAL PRACTITIONER experienced in general medicine and surgery seeking location in Minneapolis area. Individual or partnership. Write: MINNESOTA MEDICINE — 368, 496 Lowry Medical Arts Building, St. Paul 55102.

REALLY LIVE — ON THE ST. CROIX. Your own retreat. Nearer skiing — dock your boat. Spring Company has several. Contact: Harold Onstad, Marine on St. Croix, call 663-8261.

EXPANDING, UPPER MIDWEST, Multispecialty group; college city, seeks the addition of: Internist, Otolaryngologist, General Surgeon, Radiologist, and Urologist. Unlimited income. Contact: John J. Eustermann, M.D., c/o Mankato Clinic, Ltd., Mankato, Minnesota 560-387-1811.

AVAILABLE for immediate occupancy, modern doctors' offices in the Midway Medical Arts Building, University and Snelling Avenues, St. Paul. A choice Midway location near the new Inter-City Freeway with excellent public transportation available and adequate parking. Contact: Cal Douglas or Len Loftus at 646-7578-St. Paul or write Harold J. Slawik Properties, Inc., 1850 University Avenue, St. Paul.

GENERAL PRACTITIONERS — Lennox, South Dakota has exceptional opportunity available for either single practice or partnership arrangement. Lennox Clinic building available; financial, professional advantages; splendid surroundings in South-eastern South Dakota; large area to serve. Ideal for becoming established. Inquiries, visits welcome. Contact City Mayor Fred Courey, chairman, medical services committee.

"Physician interested in internal medicine wanted for Medical Service. Starting salary \$12,873 to \$17,221, depending on qualifications. Liberal fringe benefits. Non-discrimination in employment. Contact Chief of Staff, Veterans Administration Hospital, Des Moines, Iowa 50308."

WANTED — Locum Tenens, Summer, 1967, June, July and August. Board eligible in internal medicine. University trained. Write: MINNESOTA MEDICINE — 374, 496 Lowry Medical Arts Building, St. Paul 55102.

Continuation Course

Continuation Medical Education Course in OB-GYN, April 27-28-29, University of Minnesota Hospitals. Speakers: Charles Hunter, M.D., OB-GYN Department, University of Washington and John Greene, M.D., Head of the OB-GYN Department of the University of Kentucky. Contact: William Albert Sullivan, M.D., University of Minnesota Hospitals.

Minneapolis Surgical Society

The Minneapolis Surgical Society will hold its 45th Anniversary Foundation Dinner, April 6, at the Minneapolis Club. Social hour and dinner will be at 6:00. Speaker will be John Cunningham Lilly, M.D., Communications Research Institute, Miami, Florida.

Minnesota Medicine at a Glance

Insulin Preparations — Kirtley

Page 315

A whole medical generation has grown up in which the emphasis in diabetic therapy has undergone a shift and the physician can — and indeed does — feel comfortable with this concept of oral therapy that was so startlingly new ten short years ago.

In the meantime, what has happened to insulin? The answer is that it still retains its place; in fact the growth in use of insulin continues, approximating fairly closely the annual increases observed before 1955. This indicates that each year more patients are found to require insulin in treatment. But if relatively little is being written as regards the clinical use of the sulfonylureas, even less appears concerning the routine management of diabetes with insulin. This dearth of published information can be held responsible, in part at least, for some of the surprises — not to say shocks — that some of us antediluvian specimens receive when discussing problem or even routine diabetic cases in a teaching situation with younger and obviously more eager colleagues.

Pregnancy with Complicating Diabetes Mellitus — Spellacy

Page 329

The author describes the maternal and fetal complications which occur during pregnancy associated with maternal diabetes mellitus. The management of the diabetic pregnant woman and the favorable effect on the incidence of complications by maintaining good diabetic control during pregnancy are pointed out. The problem of recognition of diabetes mellitus during pregnancy is also discussed. The importance of basing the diagnosis on an intravenous glucose tolerance test and the necessity of regulating the diabetes by the frequent measurement of blood sugar levels are emphasized. It is recommended that the infants of diabetic mothers be delivered between the 36th and 37th weeks of gestation, either by induced labor or caesarean section, in order to reduce the incidence of in-utero fetal death.

The Kidneys in Diabetes — Bloodworth

Page 335

This manuscript is a review of the current status of the understanding of the pathogenesis of vascular disease and diabetes as it occurs in the kidneys. The use of the electron microscope has made it possible to obtain more details than have been observed previously.

Tick Paralysis — Medical Seminar

Page 383

Though the wood tick in Minnesota has not been reported as causing disease, it is possible for the species to be a factor in paralysis caused by the neurotoxin which can be found in the salivary gland and in the egg of this insect. In that the wood tick makes its appearance in early spring, it would be well to review the clinical manifestations of this disease.

Pseudomembranous Enterocolitis — Grand Rounds

Page 405

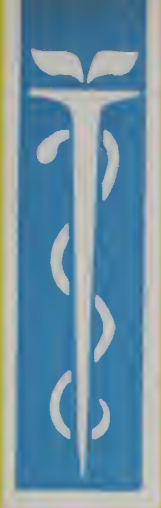
Pseudomembranous enterocolitis is an occasionally encountered critical illness in which the etiology continues to remain obscure. The disease is so fulminating and the mortality so grave that it is well worth a review of the problems as reported in Grand Rounds.

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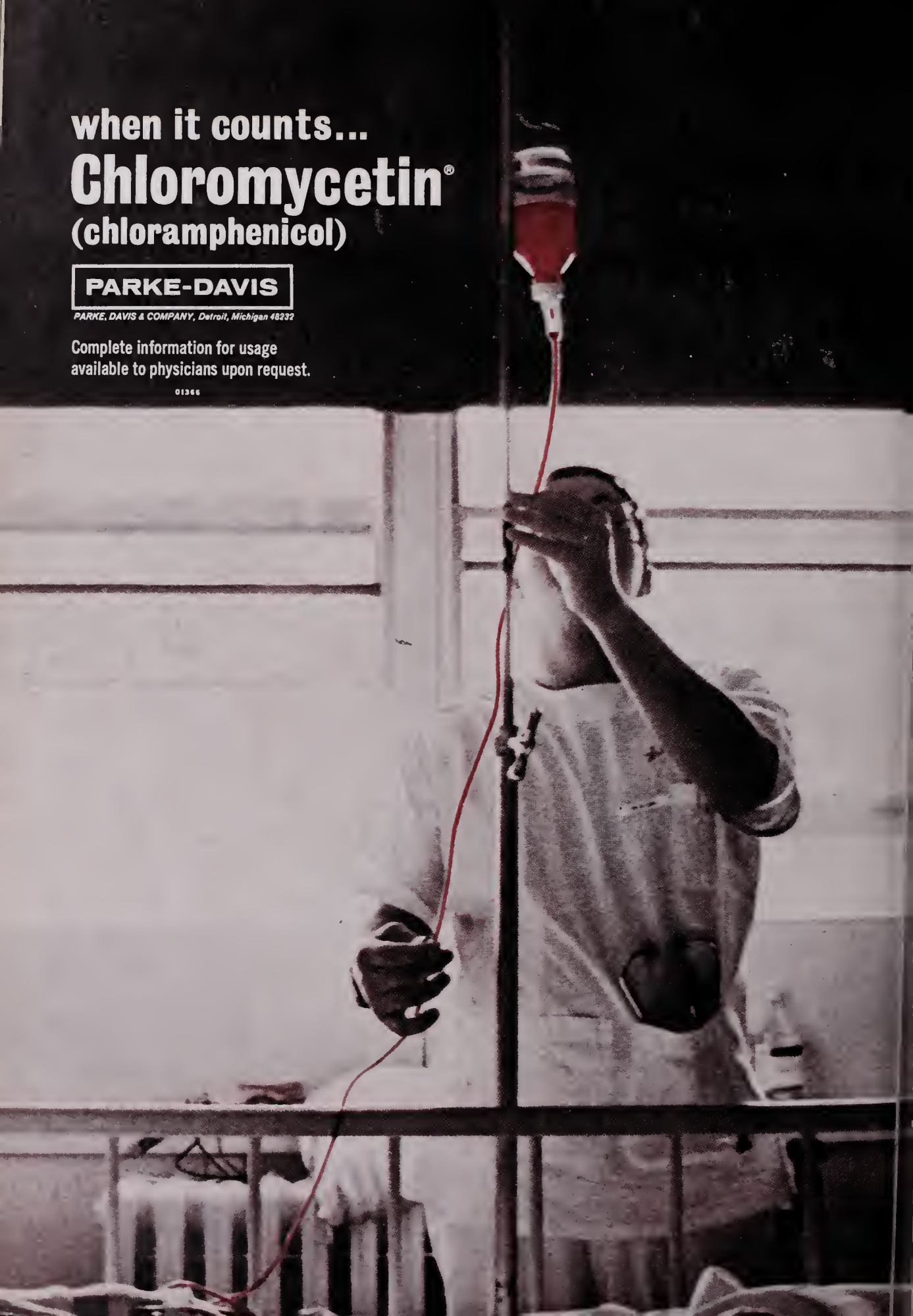
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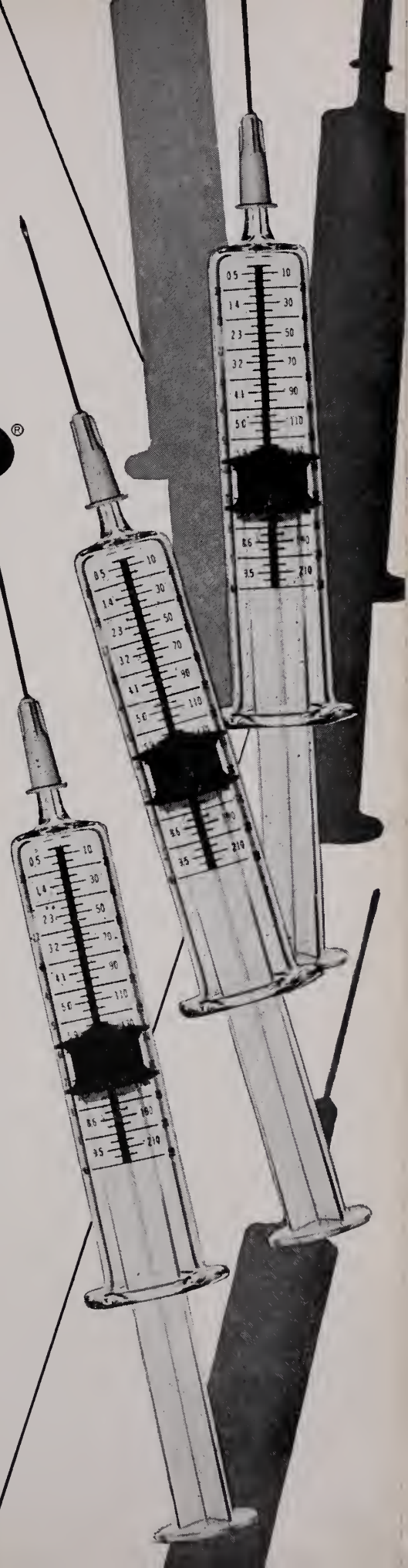
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"Snake Root" (See page 469)

W. D. Snively, Jr., M.D.

Evansville, Indiana

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President's Letter

THERE is developing an interest in a new medical school either in Rochester associated in some manner with the Mayo Graduate School of Medicine, or in St. Paul associated with the St. Paul Ramsey Hospital and the private hospitals in that city, or in Duluth.

The question of whether or not any new school, regardless of its location, shall be under the aegis of the University of Minnesota's Board of Regents is at issue. I know that tax money will probably be requested for both the building as well as the maintenance of such a new medical school. This would be in addition to the present support allocated to the University of Minnesota Medical School by the Legislature.

I believe that there is rather strong feeling on both sides of this question, and statements expressed here on this subject are strictly mine and do not represent the official opinion of the Council of the Minnesota State Medical Association.

Recently I spent some time talking with one of the officials of the American Medical Association Council on Medical Education. Some of the facts which I obtained from him are presented here:

Of the eighty-four schools listed in the 1965-1966 JAMA, Education Issue, 198:8:1066, ten are not associated with any university. Of the sixteen schools now being considered, only one is not so associated.

California, New York and Texas have multiple medical schools, all under a single board of regents. Inquiry indicated that there was intense competition among these schools, and in that official's opinion, each school was virtually autonomous.

There are at least four medical schools in the same community as their parent university but with separate campuses. About fifteen medical schools are located in different communities from the parent institution, separated by many miles. In one case, four hundred miles separates the two. All the remaining schools are on the same campus as the parent school.

It was this American Medical Association official's opinion that if a poll were to be taken of the medical school deans, the result would be a 90 to 95% vote in favor of university affiliation. He also felt that with such an affiliation it would be much easier to obtain an excellent faculty, especially in the basic sciences. It was his opinion that the faculties and students of the medical schools like to be in an atmosphere of academic excellence in related fields, such as mathematics, chemistry, physics and biology, which would be missing without such university affiliation. He also felt that the weakest schools in the country are those without such affiliation, particularly when measured in terms of faculty, graduate programs, research output and so forth.

I had started this discussion with the opinion that it would be much better to have no university connection. Obviously, I am no longer of that opinion.

C. G. Sheppard, M.D.

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Mystery of the Milksick

W. D. SNIVELY, JR., M.D.*
Evansville, Indiana

THERE ARE FEW diseases in the history of medicine that pose more puzzles than milk sickness. It is indeed "... a riddle wrapped in a mystery inside an enigma," to use Churchill's description of a quite different sort of puzzle.

But although this mystery has many facets, we can, as a result of our literature and field research, answer virtually all the questions associated with it. Here are the questions:

1. Why is milk sickness limited to the Midwest, Upper South, and Southwest?
2. Why did influential physicians on the Eastern Seaboard of the United States deny that the disease existed?
3. Why did the incidence of the disease decrease rapidly following the pioneer period?
4. Why were so few patients with milk sickness ever seen by city physicians?
5. Why do the cows whose milk causes the disease appear to be in perfect health after their calves and the humans who have drunk the milk have died?
6. How could one of this country's greatest physicians of the 19th Century, Dr. Daniel Drake, have failed to recognize the cause of the disease in spite of clear evidence?
7. Why did a world-recognized authority on bacteriology assert that the disease was caused by a bacillus in 1909?
8. How could a disease, perhaps the leading cause of death and disability in the Midwest and Upper South for over two centuries, go unrecognized by the medical profession at large until 1928?
9. How could a backwoods lady physician, inadequately trained and almost completely isolated from her fellow physicians, solve the mystery of the milksick and eradicate the

*Mead Johnson & Company, Evansville, Indiana; Clinical Professor, Department of Pediatrics, Medical College of Alabama.
Reprint requests to Dr. W. D. Snively, Jr., 2404 Pennsylvania St., Evansville, Indiana, 47721.

disease from her area almost a century before its cause was recognized by the American medical profession?

The Endemic

The milksick disease was first reported in the Midwest and Upper South in 1809. It had never been seen elsewhere — either in the United States, in Europe, or on any other continent. Certainly the pioneers along the Atlantic Seaboard knew nothing of it. If the Indians or their cattle suffered from the disease, they did not inform the early settlers. Not until the pioneers began to settle west of the mountains did the disease attract attention.

Apparently the first cases to be recognized occurred in the years shortly preceding the war of the Revolution. Then the ailment began to be seen more and more. In their opening chapter of the *History of Abraham Lincoln*, Nicolay and Hay said, "In the autumn of 1818, the new community of Pigeon Creek was almost exterminated by a frightful pestilence called the milk sickness, or in the dialect of the country, the milksick. It is a mysterious disease which has been the theme of endless wrangling among western physicians and the difficulty of ascertaining anything about it has been greatly increased by the local sensitiveness which forbids anyone to admit that any well-defined case has ever been seen in this neighborhood, although just over the creek or in the next town they have had it bad."

Because of the *milksick*, as the pioneers called it, numerous villages were abandoned. Evansville, Indiana, owes its prominent position in Indiana today, in part at least, to the fact that its early competitor, Darlington, was abandoned because of the milksick. Everything about the disease appeared mysterious except that many — perhaps most — of the persons afflicted with it died within five days to two weeks. Indeed, the mystery surrounding the ailment and its terrible fatality rate created a perfect panic among the early settlers. It was a terror that was spoken of only in whispers. Everyone denied that it had ever existed in his village or locality — up the river maybe; in the next val-

ley maybe; in a town over the ridge maybe, but *never here!* Read some quotations from early writers:

"Perhaps there is no disease [occurring with] such frequency and accompanied with such fatal results as milk sickness."

"Some of the fairest portions of the west in consequence of the prevalence of this loathsome disease must ever remain in an uninhabitable waste unless the cause and remedy can be discovered."

"Many of the finest portions of east Tennessee are known to produce this loathsome disease. Many of her most enterprising inhabitants have lost victims to it."

"No wonder pioneer families by whom malaria and typhoid were accepted as a matter of course fled back east in terror from this mysterious disease from which they died so suddenly. Their cattle and horses, apparently well, died after exercise and no one knew what it was."

"The Thomas family, our new neighbors, lost their tiny little children one September — victims to that most welcome of all childhood's nourishment — a draught of sweet milk."

"Another thing which impressed my youthful mind, although not strictly relevant to a medical article, was the hideousness of the nightly glare caused by the great fires built by the farmers to consume the bodies of their horses and cattle dead of the poison. I can never forget it."

"Horses frequently fall dead in the middle of the prairie leaving the traveler to make best of his way on foot. Cows have been known to expire in consequence of having been driven from the pasture to the barnyard."

"Danville, Indiana, has now become a perfect charnel house. No less than fifty died of milksick during the past year, and that too out of a population of 500 inhabitants."

"More than half the deaths that occurred in the early 19th Century in DuBois County, Indiana, were said to have been caused by milk sickness."

The Pharmacology

Milk sickness is really poisoning by milk from cows which have eaten white snakeroot (*Eupatorium urticaefolium*) or rayless goldenrod (*Haplopappus heterophyllus*). White snakeroot is found in the Midwest and Upper South; the rayless goldenrod, in the southwestern states, such as Arizona and New Mexico. White snakeroot is also called white sanicle, rich weed, squaw weed, snake weed, pool wort, and deer wort. It is a shade-loving plant frequently seen growing on roadsides, in damp, open areas of the woods, or on the shaded north side of ridges. The disease itself was variously designated as puking fever, sick stomach, the slows or sloes, stiff joint, swamp sickness, tires, trem-

bles* (especially as it affected animals), plus a long list of fanciful names. Poisoning by the rayless goldenrod is usually called alkali poisoning, since the rayless goldenrod grows only in extremely alkaline soils.

The Toxin

Perhaps the best designation of milk sickness is that of tremetol poisoning, since tremetol is an identified toxin that occurs in the white snakeroot and rayless goldenrod. Ether extraction of the leaves and stems of the white snakeroot produces tremetol, an unsaturated alcohol with the empirical formula $C_{16}H_{22}O_3$. In consistency and odor, tremetol resembles turpentine. The leaves of white snakeroot (don't eat too many!) have a menthol flavor; the blossoms give off a faint aroma as of lilacs.

Excretion of Toxin in Milk

Milk sickness can develop when man or animal eats the leaves or stems of the white snakeroot or rayless goldenrod, or drinks milk or eats butter from an animal that has eaten the plants. Perhaps it can occur when an animal eats heavily of the flesh or viscera of another animal that has died of severe white snakeroot poisoning. Milk secretors that ate white snakeroot were poisoned only late, since they excreted the poison into their milk.

While there is probably little white snake-root poisoning today, there may be more than health statistics indicate, since so few present-day physicians know about the disease. The correct diagnosis was made on two patients seen at the St. Louis Children's Hospital in 1963, only after they had been successfully treated for a strangely resistant acidosis. It probably would not have been made then had not the astute pediatric chief of staff remembered a patient with milk sickness whom he had seen some years before. Sporadic cases have been reported during the first half of this century. My yesterday's mail contained a letter from Dr. L. B. Newman, who wrote:

"I had a case in 1924 — white woman on small farm in east Tennessee. She had been sick 2 or 3 days when I saw her, and died 3 days later. Her most prominent symptom, as I remember,

was complete bowel paralysis, or obstipation, with resulting distention, which I was unable to relieve."

Case reports of cattle dying of trembles have reached us within the past two months. Although the disease appears infrequently in humans today, it was by no means infrequent in pioneer days. Even granting mistakes in diagnosis, the ailment might well have been the leading cause of death and disability in many Midwest and Upper South communities during the 18th and 19th Centuries. It was epidemic in dry years when cows wandered from their brown pastures into the woods in search of forage. As more forests were cleared so that cattle had adequate pasturage, even in dry weather, and as fences were built to keep the cattle in the pastures, the incidence of the disease tapered off.

It was persons who had drunk heavily of the raw milk of a severely poisoned cow who developed milk sickness. These were usually the milk lovers. When they became ill and took to their beds, appetite-depressed, energy gone, what was the food on which they chiefly subsisted? Tragically, milk! In fact, some physicians used charcoal suspended in milk as therapy. Mixing milk of several cows diluted the poison so that the toxic level was not reached. It was for this reason that little milk sickness was seen in population centers; for this reason also, city doctors almost never saw milk sickness.

Organs Affected

The severity of milk sickness relates directly to the dose of tremetol ingested. Its effects are both intense and widespread, severely affecting the liver, brain, kidneys, heart, and mucosa of the stomach and intestines. But the aspect of the disease that places the patient in the direst peril is the vicious acidosis it causes. Unless vigorously treated, this increased hydrogen ion concentration of the body fluid kills within a maximal period of two weeks. It was all that Hartmann and his group — experts in the field of acid-base disturbances with the best of modern-day facilities — could do to correct the acidosis in their two patients suffering from the ailment. The physician to-

*See Test Your Word Score Page 521.

day can but view with awe the plight in which the pioneer doctor found himself when confronted with a patient suffering from acute milk sickness.

Symptoms

In Animals

When milk sickness occurs in animals, chiefly cattle, it is called trembles. The animals suffer from anorexia, weakness, falling, stiffness, and *trembling*; hence the name. Abdominal distention and unconsciousness occur.

In Man

In man the symptoms include anorexia, listlessness, weakness, vague pains, muscle stiffness, vomiting, abdominal discomfort, severe constipation and, most important of all and underlying most of the other symptoms, profound acidosis. Because of the acidosis, the breath smells of acetone, described in days gone by as an overpowering "feter." In both man and animal, death often comes quickly. The disease can become chronic or latent; it is prone to recur if the individual is subjected to fatigue, starvation, intercurrent infection, or vigorous exercise.

The lethargy that characterizes the patient who has never completely recovered from his attack of milk sickness helped give it the name of the slows (or sloes). When Blair protested the removal of McClellan from his command, Lincoln said, "I said I would remove him if he let Lee's army get away from him, and I must do so. He has got the 'slows,' Mr. Blair."

Treatment

The modern-day physician would be correct in treating milk sickness if he attacked the acidosis vigorously. Dr. W. E. Walsh employed sodium bicarbonate in 1908, summarizing his findings in a splendid article in the *Journal of the American Medical Association* in 1926. Whether ethyl alcohol, either as such or in the form of brandy, helped cure milk sickness by neutralizing tremetol can be questioned, although several physicians endorsed beverage alcohol as a sure remedy.

The Medical Record

According to the medical literature, milk sickness probably occurred in North Carolina as early as the American Revolution, where a mountain peak today is called Milk-sick.* The Indians probably knew snakeroot poisoning as a disease of cattle, although the first published account was that of Thomas Barbee, who described it in 1809. But not until 1811 did the disease have a published name — sick stomach. The anonymous author of the 1811 article knew as much about the disorder as did most writers for a half century to come.

During the fearsome epidemic of 1818, milk sickness claimed Nancy Hanks Lincoln, mother of Abraham Lincoln; Nancy's great aunt and great uncle; and a neighbor — all at Pigeon Creek in Indiana. In searching for evidence of white snakeroot around the Lincoln cabin site at Pigeon Creek, we found one of the most dense stands we have ever seen — within a hundred yards of the cabin.

Early Research

In 1841 two erudite but unscientific publications appeared. In one of these, Dr. Daniel Drake, who had never examined a patient with the ailment, wrote at enormous length on it. He discounted the evidence produced by John Rowe, a farmer of Fayette County, Ohio, who in 1838 informed the local newspaper that he had discovered that white snakeroot was the cause of trembles in cattle. He had killed a calf and two cattle by feeding them the plant, a pig by giving it a fluid extract from crushed leaves and stems. With arrogance seldom surpassed in medical history, the great Professor Drake wrote: "A professional scrutiny only can be relied on in such cases. The testimony adduced by Mr. Rowe is, therefore, defective and inconclusive." Drake then mentioned his pet — and far from conclusive — theory, namely, that poison ivy caused the disease.

Theories of Etiology

In the years that followed, the number of theories as to the cause of milk sickness was almost as great as the number of writers.

*In the Snowbird Range, near Robbinsville, N. C.

One said the cause was arsenic; another asserted it was mysterious soil organisms; another attributed it to mysterious exhalations from the ground, and so on. Finally, in 1928, Couch reported isolation of three poisonous substances from the white snakeroot — a volatile oil and a resin acid that do not produce trembles, and an oily liquid with the characteristics of a secondary alcohol that does. The last he named *tremetol*. Since 1928, there have been nine articles published in the chemical literature on the precise chemical nature of tremetol. Thus, at long last, did the scientific community recognize in specific terms the cause of the ailment.

The importance and seriousness of the acidosis that accompanies milk sickness was recognized clinically by Walsh in 1909 and documented both with clinical observations and with blood chemical findings by Hartmann and his co-workers at Washington University in St. Louis in 1963.

A host of peculiar facts strikes one as he reads the written chronicles of milk sickness: First of all, few writers observed the highly important and characteristic fetor of the breath, which gives one the clue to acidosis, probably because so few had examined patients with milk sickness. Many authors have assumed the ailment affected the organs from which symptoms originated. Thus anorexia and vomiting, really caused by the acidosis, gave the disease the names puking fever and sick stomach. In the case of most authors, their opinions concerning the cause of milk sickness were strongly influenced by the medical fashions of the times. In addition, many authors approached the study of the disease with their minds made up as to what caused it. Fortunately, there was an exception to these general statements: a remarkable woman by the name of Dr. Anna Pierce Hobbs Bixby.

The Doctor Anna Story

Little Anna Pierce was a blue-eyed sixteen-year-old when she rode west from Philadelphia with her family in an ox-drawn covered wagon. Following the Wilderness Road, the Pierce family drove down into Kentucky, crossed the Ohio River at James Ford's

"Ferry Ohio" in 1824. But the Ford's Ferry gang coveted the blooded horses, fine cattle and nest egg of gold coins with which the Pierces hoped to buy a farm in the western country. They pursued the Pierces, who turned off the main trail into the hill country, thus escaping the robbers in a thrilling sequence of events that the old settlers in Little Egypt (Southern Illinois) still talk of around the pot-bellied stoves and fireplaces in their hilly wilderness during the winter months.

The Pierces created a farm from that wilderness not far from what later became Rock Creek Settlement in southeastern Illinois. The same farm is owned today by Clifford Joyner, who points to the site where the imposing two-story Pierce log house once stood. Anna, a conscientious youngster, was immensely disturbed by the health problems experienced by the pioneers. Determined to become a physician, she traveled to Philadelphia, where she took all the professional courses that a woman could take — courses in nursing, midwifery, and tooth-pulling. She returned to Rock Creek about 1828 to become the only physician of the community for many years.

As A Health Practitioner

As the only health practitioner in southeastern Illinois, Dr. Anna — in later years affectionately called Granny Bixby — was able to cope fairly well with the frontier ailments until an epidemic of a strange and fearsome disease ravaged the settlement. Dr. Anna quickly observed that the men and animals who were contracting the disease had invariably been drinking milk. She was deeply concerned with the ailment, which was highly fatal, and the course of which her treatment failed to influence. Her concern became even more acute when the disease killed her mother and her sister-in-law, Mary Hobbs, as well as making her father seriously ill. Anna determined to find the cause of the disease. After noticing its association with milk, she observed that the ailment was seasonal, beginning in June and ceasing after the first frost. Then she saw that although men and animals were dying of the

disease, milk cows appeared not to be affected until after those who had drunk their milk had sickened and died.

In her diary, Anna wrote, "I am convinced now that the poison which kills the calves and people saves the cows by being daily discharged through the milk glands. So, I am writing a few letters this morning and tell-



Fig. 1 — Entrance to Bixby Cave, where Eson planned to keep Anna captive.



Fig. 2 — Map showing states in which milk sickness was reported in the scientific literature during the 19th Century.

ing everyone I can to abstain wholly from milk and butter from June until after killing frosts." Then Anna saw that few horses, sheep and goats developed milk sickness. She concluded that an herb was causing the disease, reasoning thus: "Sheep and goats are careful in selecting their foods, and horses are what teachers call graminivorous; that is, grass eaters, while cattle are herbivorous and not careful in selecting. These things prove to us that it is not a grass but an herb that is spreading sorrow and death among us."

An Astute Observer

Convinced that the culprit was an herb, Anna began a systematic search of the woods. Day after day she followed the cattle, examining the plants that they ate. Then one day in the fall of 1834 her searches were richly rewarded. Early that morning, Dr. Anna had hiked into the densely forested Hobbs Ridge, carrying an herb basket, a frugal lunch, with rifle and dogs for protection. She followed the cattle, as she had so many other times, picking specimens of the herbs on which they fed. About noon, she spied an Indian squaw cowering in the underbrush. When Anna called to her to come out of hiding, the old squaw did so. Anna gave her her lunch and was delighted to find that the old woman was an Indian medicine woman fleeing from the forced migration of Shawnee Indians over the Ohio River that occurred as a result of the Treaty of 1833.

Anna took the squaw into her home, where she remained until her death many years later. The old woman soon learned of Anna's interest in the disease of milk sickness and led her to the north slope of Hobbs Ridge, where she showed Anna the white snakeroot plants that caused trembles and milk sickness. Anna gathered a basketful of the weed and showed it to her husband, Jefferson Hobbs. Jefferson, being of a practical (and skeptical) turn of mind, fed several bunches of the plant to a calf, which developed typical trembles. Now Anna was convinced that she had found the cause of the milk sickness.

Method of Eradication

Anna began a systematic program to uproot and burn all the white snakeroot in southeastern Illinois. Under her guidance, men and boys of the pioneer community carried out the program for three years, at the end of which the weed and the disease were said to have been eliminated from the area. Now white snakeroot is again extremely prevalent in southeastern Illinois, as it has always been throughout the Midwest and Upper South.

In order that doctors in other pioneer communities might learn to recognize white snakeroot, Anna raised a small crop of it in her garden. She wrote letters inviting physicians to come and examine the plant.

The second winter after Anna had shown that white snakeroot caused milk sickness, her husband died of a virulent, epidemic form of pneumonia. Overwhelmed by his death, Anna still managed to carry on her work as the only doctor in the area. She did more: she founded the Rock Creek Church, which still stands. Some years later she married a young ne'er-do-well, Eson Bixby, apparently intending to reform him. Her attempts were wretchedly unsuccessful, and Anna and her husband were separated. Later he returned and, disguised, kidnapped Anna one night, taking her to one of the seven caves of Hooven Hollow, even today one of the wildest and most primitive areas of the entire Midwest. In an effort to escape from her heartless captor, Anna leapt from the top of a cliff. Her ankle broken or sprained, she still managed to crawl into the underbrush and elude Eson. Apparently she never entirely recovered from the terrible experience. Still she continued to serve the Rock Creek Settlement as its only physician. When she died in 1869, she had received no recognition for her remarkable discovery of the cause of the milk-sick.

Delay on Identifying the Cause

Milk sickness occurred sporadically. This made it extremely difficult to make sequential observations. Next, it appeared probable that various species of white snakeroot, al-

though similar in appearance, vary greatly in toxicity. For example, careful analysis according to accepted techniques in the Mead Johnson Research Center Control Laboratory has failed to reveal tremetol in specimens of white snakeroot gathered locally.



Fig. 3 — View of the "Anna Country" from the hills to the north.



Fig. 4 — Now abandoned road over which Dr. Anna rode on horseback on her errands of mercy.



Fig. 5 — Dr. Anna and her niece, Elizabeth Ann Hobbs Foster. When Elizabeth Ann was five weeks old, Dr. Anna carried her on horseback from St. Louis, Missouri, to Rock Creek, Illinois, a distance of over 130 miles.

Third, milk secretors, such as cows, escaped poisoning early by excreting the tremetol into their milk.

Fashionable medical belief in miasmas and exhalations from the ground as causes of disease led many physicians to think that these factors caused the milksick. The disease superficially resembled arsenic poisoning, which misled others. Non-professional people, excellent observers like John Rowe, were held in disdain, while physicians like Dr. Daniel Drake, though rigid, opinionated and unobjective, were held in awe.

As the white snakeroot was sometimes infected with a bacillus and this same bacillus was found in patients dying from milk sickness, it was difficult for the physicians to believe that the bacillus was a completely innocuous plant bacillus. Indeed, in his textbook of bacteriology a famous authority attributed the disease to a bacillus.

There was a woeful lack of medical communication. Medical journals, medical societies and medical meetings as we know them today did not exist in the backwoods areas. Even in the populous centers they were in a primitive state of development. Hospitals, where physicians could meet and exchange ideas, were nonexistent until nearly the middle of the 19th Century. Because white snakeroot, hence milk sickness, was limited to the Midwest, Upper South and Southwest, influential eastern physicians refused to believe it existed.

These factors contributed to the greatest of all mysteries associated with the milksick: why it took the medical profession so long to discover the cause of the disease. In view of the complexity of the mystery, we should not be too surprised that some of the most distinguished physicians of the 19th Century, and even of the early 20th Century, failed to solve the enigma. But we certainly can be amazed that these same sources of confusion failed to keep Dr. Anna from walking down the path of accurate observation and logical reasoning that led her to the cause of the terrible plague.

Summary

In discussing Dr. Anna's remarkable discovery with my co-researcher, Louanna Furbee, I expressed the opinion that Dr. Anna made her remarkable discovery of the cause of the milksick *in spite of* her isolation and her lack of a real medical education. Miss Furbee disagreed. She felt it was *because of* Dr. Anna's isolation and lack of education. Because of her isolation, Miss Furbee pointed out, Dr. Anna had learned to depend on herself and had not developed a slavish respect for the opinions of older authoritarian colleagues. Further, because she had not been perfused with the medical theories of the time, she was able to view the ailment with objectivity.

But whether it was *in spite of* or *because of*, no one could question that Dr. Anna was a keen observer. Some persons observe specifics but neglect to see generalities. Others can see general concepts but fail to perceive individual cases. Dr. Anna was one of those rare persons who could do both. She could see the woods *and* the trees:

... She discovered that the white snake-root caused milk sickness.

... She reproduced the disease in a calf four years before farmer John Rowe did.

... She carried out the first, and perhaps the only, white snakeroot eradication program.

... She recognized the cause of the disease nearly a century before it was recognized by the medical profession as a whole.

Clearly, she was a woman of rare talents, unusual dedication, remarkable perceptivity. She richly deserved the title that was given her by her biographer, Elihu Hall, "Angel of the Ozarks."

Acknowledgments

The research project that led to the verification of Dr. Anna's role in the discovery of the cause of milksick involved many persons, who gave unstintingly of their time and knowledge. Among these were Louanna Furbee; Thomas S. Acker, SJ, Ph.D.; John W. Allen; Arthur N. Bahn, Ph.D.; Colonel George Morgan Chinn, Director, Kentucky State Historical Society; L. A. Dearinger; Ivy K. Joyner; Betty Lou Keenan; Walter Page; J. D. Quarant; and Gertrude Tyer.

Amebic Liver Abscess

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THE PRESENCE of hepatic abscesses in fatal cases of dysentery had been noted for many years, but it was not until 1887, when Kartulis in Egypt found amebae in an hepatic abscess of a patient with amebic dysentery, that the cause-effect relationship was established.²

Many have undoubtedly died from this complication of amebiasis without the diagnosis being suspected. In fact, it would appear that hepatic amebic abscess may very well have been the cause of the death of Napoleon the Great, with his gastric ulcer only an associated finding.³ The big step forward in the treatment of this worldwide disease was the discovery of the efficacy of emetine in the treatment of hepatic amebiasis by Rogers in 1912.²

Incidence

The incidence of amebiasis is, in several dozen surveys in the United States, found to be from 3-20%.² It may occur in epidemic form, as it did in the notorious outbreak in Chicago in 1933, or in sporadic case form.

Amebiasis occurs in Minnesota but is not common; however, it should be suspected in anyone who has had a gastrointestinal upset subsequent to a visit to an endemic area. Statistics differ as to the number of patients who have amebic dysentery and then develop an amebic abscess, depending upon whether it is an autopsy series or a clinical series; but 36% in the former and 11% in the latter are fairly average figures.⁴ The three cases to be presented all occurred in persons who arrived in Minnesota immediately following a stay in a foreign country. They were therefore considered prime candidates for amebiasis from the start.

Pathogenesis²

The protozoan *Entamoeba histolytica* is transmitted via the anal-oral route. There are six species of ameba parasitic in man,

but only *E. histolytica* is pathogenic. The encysted forms that survive external exposure and are ingested have walls that resist the action of the acid in the stomach but break down in the alkaline media of the small intestine, where the trophozoites emerge and penetrate the bowel wall, then gain access to the tributaries of the portal vein and are transmitted to the liver. On reaching the liver they lodge in the sinusoids, and a vigorous local reaction results — the stage of amebic hepatitis. If the amebae are not destroyed they cause necrosis

and small abscesses which coalesce to form larger single or multiple abscesses. A considerably larger number develop hepatic amebiasis than develop abscesses; apparently there is a distinct amebastatic ability of the liver to keep them in check until appropriate therapy is instituted.²

Clinical Course

The patient with a liver abscess may have it concurrent with the intestinal phase or months later. The signs and symptoms vary with the size and position of the abscess and the presence of other complicating features of the disease. Weight loss, intermittent fever, and abdominal discomfort are commonly present. Hepatomegaly may be present but jaundice is frequently absent. The presence of more than one abscess is ominous; DeBaKey and Ochsner found that in their large series of amebic hepatic abscess or hepatitis there were no known survivors of multiple abscesses.⁴ In another study of 148 fatal cases of amebiasis, 61% had hepatic abscesses.⁷ However, in this same study liver abscess as a significant cause of death was third in order, preceded by intestinal perforation and unchecked dysentery.⁷

Case Histories

Case 1

A 43-year-old man was admitted to Swedish Hospital on 8-23-65 from Lagos, Nigeria, where he had lived for the past nine months while working for an airline. Six to seven weeks prior to admission he had become ill with chills, fever, and jaundice. Hepatitis was suspected, and he was treated with antibiotics and rest with some improvement, though his general condition began to deteriorate. An x-ray of the stomach revealed a duodenal ulcer. A lesser sac abscess was suspected, and he was transferred to the United States for definitive treatment.

During his stay in the tropics he had gradually lost 28 pounds, but he attributed the loss to his difficulty in adjusting to the diet. He did not complain of diarrhea and, other than an initial spell of vomiting following a sea-food meal, he had had no gastrointestinal complaints.

Physical Findings

Physical examination revealed an acutely and chronically ill man with a large mass that was felt to be contiguous with the liver, occupying the right upper quadrant and epigastrium. He was febrile and had a gray jaundiced color. His pertinent laboratory work is seen in Table 1.

A barium enema and an oral cholecystogram were normal, but an upper gastrointestinal series re-

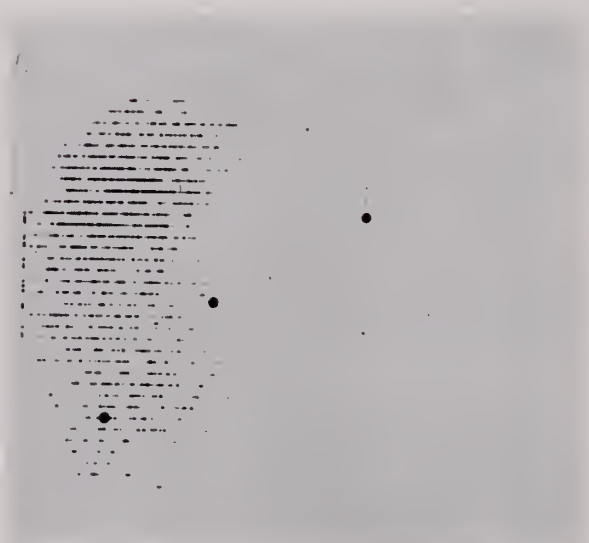


Fig. 1 — Diagnostic liver scan showing large left lobe space-occupying lesion.



Fig. 2 — Operative Skiodan study of cyst.

vealed an active duodenal ulcer crater, and the stomach was displaced to the left and anteriorly by a mass. Although a lesser sac abscess was a definite possibility and in spite of the fact that several stools were negative for ova and parasites, a neoplastic process or cyst in the liver was thought to be a possibility. An Au¹⁹⁸ liver scan (Figure 1) was performed, revealing the right lobe to be normal but a large space-occupying lesion to be present in the left lobe.

TABLE 1

	Case 1	Case 2	Case 3
Sedimentation rate	103	80	122
WBC	14,600	16,700	16,300
Hemoglobin	11.2	13.4	11.1
Bilirubin	0.6/2.4	0.4/0.9	0.4/1.1
Ceph floc	3+	—	3+
Alk P'tase	39	19.2	7.8
A/G ratio	2.8/3.7	3.3/3.3	2.4/3.6
Pro time	11.4/14.0	—	14.0/15.0
Bromsulphalein	—	30%	12%
T.T.	—	1	—

Surgical Management

At surgery the left lobe of the liver was remarkably enlarged and slightly darker in color, but its capsule appeared normal. Needle aspiration deep into the left lobe revealed a slightly hemorrhagic, grayish purulent matter to be present. Repeated aspirations with a #13 needle resulted in the removal of 1300 cc. of pus. Injection of Skiodan into the cavity (Figure 2) revealed it to correspond to the left lobe space-occupying lesion as seen on the preoperative liver scan. A #20 Foley catheter was placed in the cavity, brought out through a stab wound, and subsequently connected to straight drainage.

All laboratory studies on the aspirate revealed

only a para colon bacillus on sub culture. No biopsy of the abscess wall was obtained — nor was it feasible to obtain scrapings. However, serum sent to the State lab showed a *positive* hemagglutination test for amebiasis. Postoperatively the patient was treated with emetine 65 mgm. daily × 5 and chloroquine 250 mgm. q.i.d. × 21 days. He was also treated medically for his duodenal ulcer. His recovery was rapid and he was discharged on 9-9-65. Six months later he wrote from Nigeria stating he felt well and had regained his lost weight.

Case 2*

A 55-year-old male was admitted to Swedish Hospital on 3-30-66 because of fever and chills for five days prior to admission. He had been started on tetracycline and penicillin, which had not affected his temperature.

His symptoms had begun about one week after his return from a vacation in Mexico. During his stay there he had suffered at times from bouts of mild gastroenteritis. On admission he was having frequent and loose blood-tinged stools. However, on repeated examination of his stools neither trophozoites nor cysts were seen.

Physical Findings

Physical examination revealed a mild tenderness to palpation in the right upper quadrant.

It was suspected that the patient might have a liver abscess in spite of the negative stool findings, and a liver scan with Au¹⁹⁸ was ordered. This revealed two definite areas of decreased pick up, one in the right lobe and one in the left lobe.^{xx} (Fig. 3) Liver abscesses or metastatic tumor in the liver were suspected.

Surgical Management

He was started on emetine, chloroquine, and Duquaine therapy on 4-3-66, and on 4-11-66 his abdomen was explored through a right subcostal incision. The liver was characterized as having a darker than

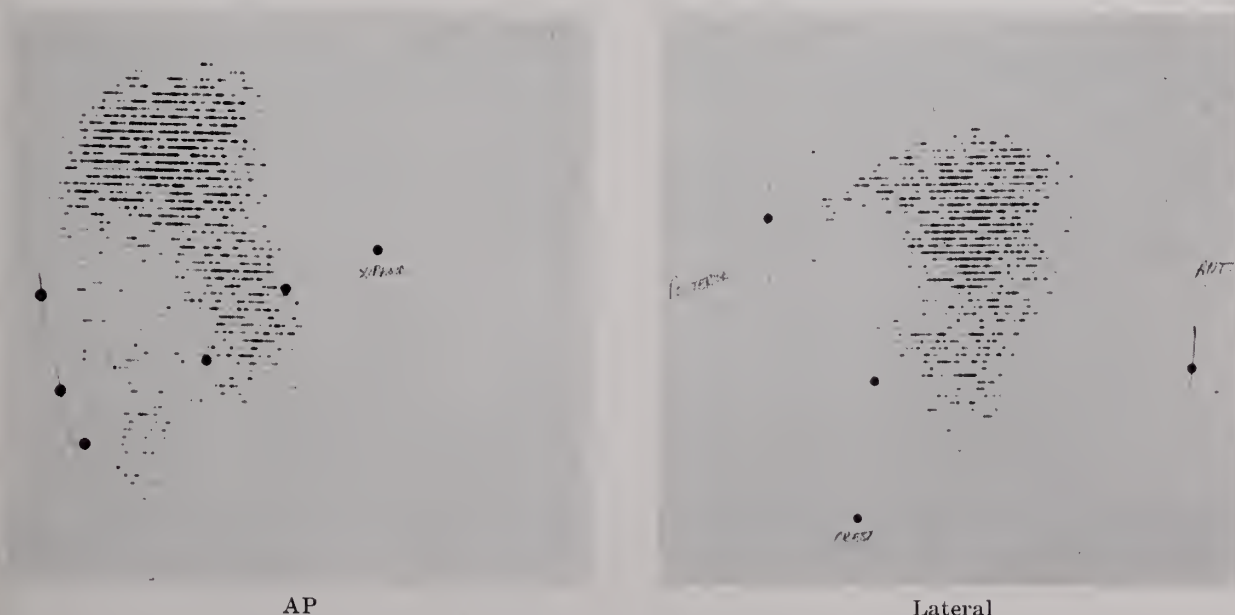


Fig. 3 — Preoperative Au¹⁹⁸ liver scan showing multiple space-occupying lesions.

normal color. Aspiration with a #13 needle in several places where bulging was noted revealed three distinct cavities containing 70, 40, and 60 cc. of "anchovy paste" pus. Two abscesses were in the right lobe and one was in the left. Penrose drains were placed close to the puncture sites and one cavity was curetted.

No cysts, trophozoites, or bacteria were found in the scrapings, but the course of anti-amebic medical therapy was completed. He made an uneventful recovery and was discharged on 4-26-66. The clinical history, type of material found, and rapid response to anti-amebic therapy make the diagnosis of amebic liver abscess quite likely.

Case 3

A 40-year-old female missionary returned to the United States after 3½ years of service in Mexico. Six days before admission to Swedish Hospital she developed mild indigestion, anorexia and right upper quadrant pain. When her symptoms persisted she was admitted on 8-28-62.

Physical Findings

No jaundice was present, but there was tenderness to palpation in the right upper quadrant, although no mass was felt. She had had amebic dysentery earlier during her stay in Mexico, but this was successfully treated. The initial diagnosis after all studies had been completed was cholecystitis; but amebic liver abscess was considered a likely possibility.

A proctoscopic examination was unremarkable, but trophozoites of *Entamoeba histolytica* were seen on examination of a stool specimen. On 8-30-62 she was started on emetine and chloroquine therapy.

Surgical Management

At surgery on 9-1-62 a right subcostal incision was utilized to explore the right upper quadrant. The gall bladder was normal, but the dome of the right lobe of the liver was adherent to the diaphragm. Blunt dissection in this area revealed a 4 × 5 cm. cavity containing pus. After evacuation of the purulent matter a mushroom catheter was placed in the cavity and brought out through a stab wound.

There was no growth on culture of the material. A course of emetine and chloroquine was completed following surgery and all stools became negative for trophozoites or cysts. She was discharged from the hospital and has been followed for four years with no recurrence of her symptoms.

Discussion

Amebiasis should have been suspected preoperatively in Case 1 simply because the patient came from the tropics. Neither trophozoites or cysts were found in Cases 1 and 2, but this should have been followed up by proctoscopic examinations. Even though diarrhea may not be present, small ulcerations may be seen, and scrapings from these areas frequently reveal the ameba when the stool

does not.⁶ Usually cysts are discovered in formed stools, whereas trophozoites are seen in watery stools.⁶

Eosinophilia is not commonly present, although it was observed on one differential in Case 2. The wbc. is usually elevated along with the sedimentation rate. This was true in all three cases presented. It seems that the clinical deterioration is correlated with the amount of pus present in the liver. The patient (Case 1) who had a cyst containing 1300 cc. was extremely ill. The presence of jaundice is variable and not particularly helpful in making the diagnosis. Although liver cellular tests may be abnormal, they are of little help in deciding whether an abscess is present as opposed to amebic hepatitis.

Liver-scan studies utilizing Au¹⁹⁸ or Rose Bengal¹³¹ as originally described by Friedell⁵ are of great assistance in determining whether an abscess of significant size is present in the liver. Scans were done on two of our patients and were helpful in localizing the abscess. If there is a single abscess close to the surface of the liver it may be aspirated percutaneously. If open aspiration is to be done the choice of incisions is aided. Serial scanning of the patient in his convalescent course may be done to determine resolution of the abscess cavity. An Au¹⁹⁸ liver scan subjects the liver to approximately 0.5 to 3.5 r. irradiation; this is in contrast to 9 r. on a cholografin examination of the gall bladder.¹

Closed vs. Open Aspiration

The advantages of open over closed aspiration are illustrated in the three cases presented. Closed aspiration of Case 3 would have had to be through the pleural cavity and would have risked contamination of this space. In Case 2 there were three distinct abscesses. It seems unlikely that they could have been localized as well and drained as completely through the percutaneous route as through an open incision. The position of the abscess deep in the left lobe in Case 3 makes difficult a successful percutaneous aspiration. It should be said, however, that closed percutaneous aspiration is superior to open aspiration if the abscess cavity can be

accurately localized close to the surface of the liver.¹

Medical Treatment

It does not seem unreasonable to assume that considerable pus may remain after aspiration. This certainly seems likely in Cases 1 and 2. Yet the patients made prompt and complete recoveries. This we must attribute to the efficacy of emetine and adjuvant anti-amebic therapy. Many cases of hepatic amebiasis with micro-abscesses are undoubtedly cured by these efficacious drugs before reaching the large abscess stage.⁴ It should be emphasized that emetine therapy is not without its hazards, and close clinical scrutiny must be maintained during treatment.

Finally it should be added that amebic hepatic abscess is only one of many serious complications that can follow amebic dysentery. Ulceration and perforation of the colon with peritonitis, stricture formation with obstruction, appendicitis, rectal ulceration and fistula formation, and other extra-intestinal areas of involvement (i.e., lung) can all occur and may be more devastating.²

Summary

Amebiasis is notorious for its wide-spread distribution. Amebic hepatic abscess is one of several complications that may occur following amebic dysentery. Three cases of amebic hepatic abscess were successfully treated by open surgical drainage and anti-amebic medical therapy.

References

1. Block, M. A., Schuman, B. M., Eyler, W. R., Trueant, J. P., and DuSault, L. A.: Surgery of Liver Abscesses. *Arch Surg* 88:4:602, 1964.
2. Cahill: Tropical Diseases in Temperate Climates. Lippincott, Philadelphia and Montreal. p. 92, 1964.
3. Cawadias, O. B. E., A. P.: The Fatal Illness of Napoleon the Great. *Amer Heart J* 65:2:277, 1963.
4. DeBakey, M. E., Ochsner, A.: Hepatic Amebiasis, *Int Abstr Surg* 92:3:219, 1951.
5. Friedell, H. L., MacIntyre, W. J., Rejali, A. M.: A Method of the Visualization of the Configuration of the Liver. *Amer J Roentgen* 77:3, 1957.
6. Healy, G. R.: The Laboratory Diagnosis of Amebiasis. *Amer J Gastroent* 42:2:191.
7. Kean, B. H., Gilmore, Jr., H. R., Van Stone, W.: Fatal Amebiasis Report of 148 Fatal Cases from the Armed Forces Institute of Pathology. *Ann Intern Med* 44:5:839, 1956.

Green Medicinals

Herbs for the Reproductive Organs

Ecclesiasticus said: The Lord hath created medicines out of the earth and a wise man will not abhor them. To benefit the reproductive organs herbalism proffers arbor vitae, burdock, eryngo, groundsel, marjoram, pennyroyal, tansy, and wild thyme.

Besides being wholesome, tansy fritters sound appetizing:

Tansy Fritters

Take the crumbs of a small loaf of bread, pour on it half a pint of boiling milk; let it stand an hour, then put in as much juice of tansy as will give it a flavour, but not to make it bitter, then make it a pretty green with spinach juice, put to it a spoonful of ratafia* water, or brandy. Sweeten it to taste, grate over it the rind of half a lemon, beat the yolks of four eggs, mix them all together, put them in a tossing-pan, with four ounces of butter, stir it over a slow fire till it is thick, take it off and let it stand two or three hours, then cut into fritters and drop them into a pan of boiling lard; a spoonful is enough for a fritter. Serve them up surrounded by slices of orange, grate sugar over them, and serve a wine sauce separately. — Elizabeth Raffald (1825)

*See Test Your Word Score Page 521.

From Hufeland's Makrobiotik*

On the 2nd of August, 1790, a carabinier named Petit jumped into the river from one of the windows of the Military Hospital at Strassburg. Half an hour later, — as nearly as could be learned from an inquiry that was made at the time of the occurrence, — his body was taken from the water and carried into the hospital. To all appearances the man was dead; no evidences of life were discovered. Nevertheless, efforts were made to revive him. The body was placed in a thoroughly warmed bed, with the head lying high up on a pillow, the arms resting on the trunk, and the legs extended side by side. The only other measures adopted were the following: At short but regular intervals of time heated cloths were placed over the region of the stomach and over the legs; and heated stones wrapped in cloths were placed in different parts of the bed. At the end of seven or eight minutes a slight twitching of the man's upper eyelids was observed, and a short time afterward his lower jaw, which up to that moment had been in firm contact with the upper jaw, became separated from it and permitted a little frothy mucus to escape between the lips. After this discovery had been made, a little wine was cautiously introduced into the man's mouth. Apparently it was swallowed, and then other small doses of wine were administered, all of them apparently being swallowed. Under this stimulation the pulse beats at the wrist became perceptible, and at the end of one hour the man was able to answer questions.

— Christoph Hufeland (1762-1836)

**See Test Your Word Score Page 521.

Buckle Up

Highway Hypnosis

Among the most frequent causes of accidents on freeways is highway hypnosis — the purr of your engine; the hum of your tires; the white ribbon of highway unfolding endlessly ahead; the hypnotic sameness which lulls you into a trance.

You gain a false sense of security. You're not aware of traffic conditions around you. In a sub-alert state you may doze at the wheel or drive off the road. You lose your ability to judge speed and distance.

You can combat highway hypnosis by:

Stopping often to freshen up and check your car. Frequent stops not only enable the motorist to refresh himself, but allow time for dissipation of heat built up by tires during continuous high-speed driving. While you are stopped, wash up — have a bite to eat — walk around — take a nap — get gasoline — have some coffee — NOTHING STRONGER!

You can also help yourself to stay awake by checking your speedometer often — keeping a window open for fresh air — avoiding a fixed eye position by keeping the eyes moving — listening to lively radio programs — chewing gum — singing and talking aloud — cracking a smile to ease the strain — changing drivers often — eating lightly — keeping your mind active by concentrating ahead — and being interested in what's going on outside your car.

A New Intra-Articular Steroid

**with
Prolonged
Anti-
Inflammatory
Action**

PAUL J. BILKA, M.D.*
Minneapolis, Minnesota

THE INTRA-ARTICULAR use of adrenocorticosteroids is an established and valuable therapeutic tool in the management of many rheumatic disorders.¹ In rheumatoid arthritis it is useful as an adjunct in the patient whose active synovitis is limited to or is especially severe in one or a few joints. If hydrocortisone acetate is injected into an active rheumatoid joint, marked reduction or complete relief of local inflammation can be expected to occur within 24 hours and to last for an average of one to two weeks. If a more insoluble ester of hydrocortisone is injected, namely hydrocortisone t-butyl acetate, similarly rapid improvement can be expected, but the duration of effect is lengthened two or three-fold to an average of four weeks.² Various modifications of multiple steroid analogs** have failed, to the present time, to materially improve upon the effectiveness of hydrocortisone t-butyl acetate. An exception is the brief report by Hollander et al. in 1961.³ The purpose of this report is to present data on a new steroid that has a significantly prolonged local anti-inflammatory effect in patients with rheumatoid arthritis.

Present Study

One hundred and twenty-five patients with active rheumatoid arthritis were selected as test subjects for the new steroid. All patients met the American Rheumatism Association criteria for the diagnosis of either definite or classical rheumatoid arthritis. All injected joints had objective clinical evidence of swelling as demonstrated by free fluid or synovial thickening and all demonstrated synovial tenderness. Joints with inactive disease, or with largely destructive or me-

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**See Test Your Word Score Page 521.

chanical changes were not included in this study.

The drug used is triamcinalone hexacetonide, which differs from the parent compound triamcinalone by possessing an acetonide group at C-16 and C-17 and a tertiary butylacetate radical at C-21 instead of free hydroxyl groups at these carbon atoms. This modification makes the compound much less water-soluble, thereby prolonging its duration of action. The drug was provided as a fine crystalline suspension containing 20 mg. of triamcinalone hexacetonide per cc. of solution.* Unless otherwise stated, one cc. of the suspension was injected into each joint.

Degree of Relief

The 125 patients were given 289 separate injections of triamcinalone hexacetonide as detailed in Table 1. The initial post-injection examination was usually made at one week, with subsequent examinations at one to four-week intervals. Joint swelling and tenderness were recorded on a grade zero to four basis, and range of motion was recorded in degrees. A statement from the patient of an estimate of the local joint improvement was recorded, and was usually supportable by "objective" criteria such as ability to walk without a limp, ability to turn a faucet or door knob with one hand, etc. In the case of the one patient who had two hip-joint injections, the assessment of improvement was based on her subjective estimate, plus range of hip motion, inasmuch as palpation of the hip synovium is rarely possible.

Following 267 injections, or in 92.3%, the patient obtained over 90% local symptomatic relief plus objective reduction in joint swelling and tenderness. In seven injections, or in 2.4%, the result was listed as poor — or less than 25% relief. Four of these seven poor results followed ankle injections. Two injections (0.8%) were classified as "good," with 50% to 90% relief, and 13 injections (4.5%) were classified as "fair" with 25% to 50% relief. These results are not too different from those reported by other authors using several other types of intra-articular steroids.

*Supplied by Lederle Laboratories, Pearl River, New York.

Duration of Relief

This was the next significant feature studied and the details are presented in Table 2. Only the 267 injections with an initial "excellent" response are here analysed. When an injected joint begins to lose its local anti-inflammatory effect, it returns to its pre-injection state rather rapidly, usually within one week. In this assessment, as soon as a joint went below 90% improvement it

TABLE 1
Injection Sites In 125 Patients And Response

Joint	Number of Patients	Number of Injections	Number and % of "Excellent" Response*
Knee	98	194	189 (97%)
Elbow	23	32	31 (97%)
Wrist	15	18	16 (89%)
Finger**	11	22	22 (100%)
Ankle	8	13	5 (38%)
Shoulder	4	8	3 (38%)
Hip	1	2	1 (50%)
Total	†	289	267 (92.3%)

*"Excellent" response is greater than 90% relief of local joint inflammation.

**0.5 cc. or 10 mg. of triamcinalone hexacetonide used for finger joint injections except for 2 injections of one cc.

†Total more than 125 since some patients had more than one site injected.

TABLE 2
Duration Of Relief In 267 "Excellent" Responses

Joint	Less Than 1 Mo.	1 to 3 Mos.	Longer Than 3 Mos.
Knee	14	90	85
Elbow	1	7	23
Wrist	0	6	10
Finger	0	4	18
Ankle	1	2	2
Shoulder	0	1	2
Hip	0	0	1
Total	16	110	141

TABLE 3
Comparison Triamcinalone Hexacetonide With Hydrocortisone t-Butyl Acetate

	Patients Trials	
Triamcinalone hexacetonide and hydrocortisone TBA both ineffective	1	1
Triamcinalone hexacetonide shorter duration than hydrocortisone TBA	1	1
Triamcinalone hexacetonide and hydrocortisone TBA equal duration	15	32
Triamcinalone hexacetonide longer duration than hydrocortisone TBA	58	92

was recorded as at the termination of its "excellent" response. It is seen that in over half of the injections the full benefit lasted for longer than three months, and in only 6% did the "excellent" response last for less than one month. It may be of interest that the non-weight bearing joints appear to have a greater percentage of long lasting results. This could reflect the effect of trauma in causing an earlier return of inflammatory signs to a weight bearing joint.

Reactions

There were seven instances, in seven patients, of increased local pain or inflammation following the injection with triamcinalone hexacetonide. Three of these followed finger injections where the volume of material (0.5 cc. in two instances and 1 cc. in another) injected into a small joint could have played a traumatic role. Two reactions followed ankle injections, and one each followed a wrist and an elbow injection. Three of the reactions were relatively mild, and all seven post-injection flares subsided within four days following only symptomatic therapy. Five of these patients had other joints injected with triamcinalone hexacetonide without local reactions. The cause of these transient flares is uncertain, but very likely the trauma of the injection is a factor. McCarty and Hogan have also suggested the role of a foreign body type reaction to corticosteroid crystals.⁴

Systemic Effects

It is not uncommon, following an intra-articular injection of hydrocortisone acetate, or especially one of its more potent soluble analogs, for patients to experience a generalized subjective or objective improvement of mild to moderate degree lasting for as long as several days. This is believed to be due to systemic absorption of the drug, but how much is due to psychogenic influences is uncertain. With the use of hydrocortisone t-butyl acetate these systemic responses are minimized. Although each cc. of triamcinalone hexacetonide contains 20 mg. of a potent adrenocorticoid which is the equivalent of 100 mg. hydrocortisone, it is postulated by the manufacturers that the insolubility of

the compound is unlikely to cause significant systemic effects from absorption at the injection site. Nevertheless, 26 patients on 35 occasions reported at least 25% improvement in their other joints plus a feeling of systemic well-being following joint injection with triamcinalone hexacetonide. In seven of the 35 instances, 2 cc. or 40 mg. triamcinalone hexacetonide had been injected at one sitting, and in one instance a total of 3 cc. was given in multiple joints. It is difficult to escape the belief that significant systemic absorption has occurred in most of these patients. With this in mind the drug should be used with the precautions of potential overuse attending all adrenal corticosteroids, whether given locally or systemically.

Comparison with Hydrocortisone

The final feature of the study of the new compound was to compare its effectiveness with hydrocortisone t-butyl acetate. One hundred twenty-six trials were performed in 73 patients. A trial consisted of the observations associated with the injection of one cc. hydrocortisone t-butyl acetate (25 mg. hydrocortisone) or one cc. triamcinalone hexacetonide followed by a later injection of the alternate drug when the local signs of joint inflammation returned to their pre-injection state. Table 3 presents a summary of these observations. Both compounds gave an equally high percentage of initial "excellent" responses and in 25% of the trials this response was of equal duration for the two drugs. In 92 instances, or 73.6% of the total trials, triamcinalone hexacetonide had a 25% or longer duration of the local anti-inflammatory effect when compared with hydrocortisone t-butyl acetate. In 79 of these instances, or in 85.8%, this longer duration was by a factor of at least two, and in 54 trials, or 59.7%, the duration was at least three times longer with triamcinalone hexacetonide. Over all, the mean duration of effect was one month for hydrocortisone t-butyl acetate and three months for triamcinalone hexacetonide.

Summary and Conclusion

Triamcinalone hexacetonide, a new insoluble adrenocorticoid, was given 289 times

by intra-articular injection to 125 patients with active rheumatoid arthritis. In 267 trials, or 92.3%, a 90% or greater reduction in local inflammation was obtained, thus demonstrating an effect comparable to other reported cortisone analogs. However, in 141 trials, or in one half the injections, this local anti-inflammatory effect lasted for longer than three months. Transient local reactions occurred in seven instances (2.4%) and clinical evidence of systemic absorption followed

35 trials (12%). In a direct comparison with hydrocortisone t-butyl acetate in 73 patients and 126 trials, the new compound had a longer duration in 73.6% of the trials. The mean duration of local anti-inflammatory effect for hydrocortisone t-butyl acetate was one month, and for triamcinalone hexacetonide it was three months. Triamcinalone hexacetonide appears to offer a significant advance in intra-articular therapy in rheumatoid arthritis.

References

1. Hollander, J. L.: Intrasynovial Corticosteroid Therapy. Chapter in "Arthritis and Allied Conditions" p. 381. Lea & Febiger, Phil. 1966.
2. Bilka, P. J.: A New Hydrocortisone for Intra-Articular Use. *Minnesota Med* 38:408, 1955.
3. Hollander, J. L., Jessar, R. A., Restifo, R. A., and Fort, H. J.: A New Intra-Articular Steroid Ester with Longer Effectiveness. *Arthritis Rheum* 4: 422, 1961.
4. McCarty, D. J. and Hogan, J. M.: Inflammatory Reaction after Intrasynovial Injection of Microcrystalline Adrenocorticosteroid Esters. *Arthritis Rheum* 7:359, 1964.

The Frontier Doctor — I

On the frontier a doctor was ranked with the schoolmaster, the minister and the judge. When he rode out to see the sick, boys lifted their hats to him and girls curtsied. In many parts of the West even the settlers' vicious dogs were not allowed to snap at the doctor as he cantered by. The physician was conceded the right to shoot a dog if he proved a nuisance. In the Far West bandits and rustlers let the doctor ride by unharmed. After all, a man never knew when he might desperately need his services.

All of this did not mean that the pioneer doctor was universally honored on the frontier, for there were many frontiersmen who hated him simply because he was an educated man. Some sniggered and repeated the popular saying, "The boy who goes into medicine is too lazy for farm or shop, too stupid for the bar, and too immoral for the pulpit."

— Richard Dunlop: *Doctors of the American Frontier*, Doubleday, 1965.

Abdominal Migraine Syndrome

Various writers have classified as a syndrome the symptoms of abdominal pain, nausea, vomiting, and sometimes diarrhea that are frequently a conspicuous part of the clinical picture of migraine (Brams, Blumenthal). The abdominal migraine syndrome is seen primarily in children or in adults who have had migraine for many years. Typical is a history of colic as a baby and a family history of headache or biliousness or both. Not infrequently the abdominal symptoms continue during childhood without attacks of headache, or may alternate in their occurrence with attacks of cephalalgia, or may continue after the headache has ceased. Parenteral administration of ergotamine usually causes prompt subsidence of symptoms. Desensitization with intravenous histamine affords more prolonged relief.

Durham, Robert H. — *Encyclopedia of Medical Syndromes*
Hoeber Medical Division, Harper and Row, New York

Restoration of Cerebral Physiology

An Unusual Case of Cardiac Resuscitation

LEROY EKSTRAND, M.D.*
Wabasha, Minnesota

DR. LEROY EKSTRAND'S report,** "Restoration of Cerebral Physiology: An Unusual Case of Cardiac Resuscitation," is of unusual interest for several reasons.

Not only is the case noteworthy because of the way the patient was treated and the results which followed, but it is an example of excellent medical practice in a small Minnesota community by a conscientious, knowledgeable physician, a member of a small professional group practicing in the community. Also, when hospitalization was necessary, the fine Community Hospital, St. Elizabeth's, with its nursing staff, assisted admirably in the care of the patient.

Dr. Ekstrand, with the assistance of Wabasha firemen whom he had trained in resuscitation methods, restored temporary cardiovascular function in two other cases. But both patients had been under water for an extended period of time, and cerebral damage was so severe from the anoxia that they died after eight to 14 hours of cardiovascular-pulmonary activity.

Dr. Ekstrand died last August from diffuse intestinal bleeding complicating a diffuse arteritis.

Waltman Walters, M.D.
Rochester, Minnesota

A 55-year-old white female school teacher had been feeling well until the night of April 22, 1965, when she awoke at 2 a.m. with severe substernal pain which radiated down both arms and was associated with shortness of breath. About half an hour later when seen in the home she was still having severe pain in the substernal area, but the pain seemed to be easing somewhat. At that time the patient's color was good and she was able to give a history which was typical of the pain of myocardial infarction. She had been hypertensive since 1961 and had been taking Diuril since that date. When last taken in the office, her blood pressure was 136 mm. Hg. systolic and 100 diastolic and she was taking Diuril, 500 mg. in the morning, and Eutonil, two tablets in the evening.

It so happened that this attack occurred during the time when the city of Wabasha was flooded, and in order to get the patient to the hospital she

*Community Clinic.
**Posthumous.

would have had to be transported by army truck across flooded roads. She was given 100 mg. of demerol, which made her fairly comfortable, and her husband was told to notify the physician if her symptoms became worse. About an hour later she began to have more pain; so an ambulance was summoned with the idea of taking the patient to the place where the ferry service with a truck could be used to transport her to the hospital. The ambulance driver and the physician arrived at the patient's side at about the same time.

The patient appeared moribund, pale, cyanotic, in cold perspiration, pulseless, and with only an occasional isolated shallow breath. She was unconscious and limp, but her pupils were not yet dilated.

Emergency Procedures

She was immediately removed from the bed to the floor where external cardiac massage and mouth-to-mouth respiration were begun. A plastic airway was inserted, and the patient's legs were elevated on a chair. While the ambulance driver, who was experienced at cardiac massage, continued the resuscitation, one ml. of Aramine was injected intravenously. After about five minutes of these efforts the patient seemed to respond favorably and started to breathe in gasps of about seven or eight per minute. However, no pulse could be felt when the cardiac massage was temporarily stopped.

On several occasions the respiration and color seemed to be improving so much that cardiac massage was stopped long enough to listen to the heart and feel for the pulse. When this was done the respiration deteriorated again, and no pulse or heart beat was evident until the massage was resumed. During massage a definite pulse could be felt with every pressure on the chest. Oxygen from the ambulance was then administered nasally. This seemed to improve the patient's color somewhat. External cardiac massage was used at a rate of about 40 per minute.

When the patient started to breathe spontaneously, an attempt was made to time the pressure on the chest so that it would occur between the inspirations. Soon the patient was breathing fairly well, but when the cardiac massage was stopped the respirations again deteriorated. After about 45 minutes of resuscitation, it was felt that if the patient could not continue on her own, further resuscitative measures would be futile. The cardiac massage was stopped; at this time a feeble pulse could be felt and the respirations were continuing. The pulse became stronger and quite regular. The blood pressure increased to 110/90, the color improved, and respirations became more normal. The patient was then transported to the hospital in an army truck with the oxygen going continuously. During the trip she remained unconscious and was perspiring profusely. She arrived at the hospital at 4:15 a.m. with a blood pressure of 100/60. At 4:45 a.m. she was moaning and restless with pain. After 0.5 ml. of Aramine was given intramuscularly, the blood pressure increased rapidly to 160/110, but subsequently the pressure decreased again to shock levels.

Hospital Management

On admission the patient was given sodium bicarbonate; heparin, 500 units every four hours intravenously; Aramine, 0.5 ml. intramuscularly as indicated (when systolic blood pressure was less than 100); and oxygen. Pulse, blood pressure, and respirations were followed closely. She was also given morphine sulfate, 1/6 grain, as indicated for restlessness, and penicillin, 500,000 units every 12 hours. She was catheterized so that the urinary output could be followed. The next morning she was semiconscious and in a cold sweat. The heart rhythm was irregular and the rate rapid. Breathing was easy. At 1:30 p.m. the blood pressure dropped to 80/70 and she was perspiring freely again. Levophed was given; this brought the blood pressure up to 110/80, and it was maintained at that level with the use of Levophed.

Results of laboratory tests on this day included the following: For blood, hematocrit, 47%; hemoglobin, 14.7 gm.; white blood cell count, 17,100. Urinalysis showed 4+ albumin and a trace of sugar; specific gravity was 1.020; reaction was acid; and the specimen was packed with white blood cells, epithelial cells, and some granular casts. The results of subsequent laboratory tests are given in the Table. The electrocardiogram of April 23, the day after the attack, showed many premature ventricular contractions, some occurring in runs and having varying foci from which they originated, Q waves, T waves, and ST shifts suggestive of massive myocardial infarction.

Progress

The next day she was able to open her eyes and smile and take water from a straw. The electro-

Results of Laboratory Tests

April 25

pH 7.34
Calcium 5.9 mg/100 ml.
Sodium 134 mEq/liter
Chlorides 105 mEq/liter
CO₂ 21 mEq/liter

April 27

pH 7.35
Sodium 136 mEq/liter
Potassium 5.2 mEq/liter

April 29

Urine (catheterized)
Marked clearing
Trace of albumin
10 wbc. per high-power field

May 6

White blood count 13,200/cu. mm.
Hemoglobin 13.1 Gm.
Sedimentation rate 19 mm. in 1 hour
Serum transaminase 26 units

May 17

Hematocrit 39%
Hemoglobin 12.6 Gm.

May 26

Cholesterol 131 mg/100 ml.

cardiogram was abnormal but showed improvement over the previous one. Her skin was warm and her chest was clear. She had a urinary output of 300 ml. Three days after admission she was taking water out of a glass and could smile and answer "yes" or "no." The fourth day she appeared brighter, and her blood pressure was staying above 100 mm. systolic without stimulants. Her chest was clear and her heart regular. That night she had to be catheterized again because of an overflow type of urination. An electrocardiogram on April 28 was compatible with recent, healing posterior myocardial infarction. Five days after admission she was able to read the headlines of the newspaper but was unable to tell who she was and was unable to give her husband's name. On the eighth day a foot drop was noted in the left foot. Urecholine had been necessary because the patient had been unable to void after catheterization, but on the twelfth day she was able to void on request.

End Result

After two weeks in the hospital she still had difficulty with her memory and was still unable to name her physician or even her husband. Three weeks after admission she was able to feed herself and carry on a fairly good conversation but was still unable to remember names or places. The blood pressure at that time was 116/80 and the pulse was regular, but the foot drop persisted. The electrocardiogram at that time showed a healing posterior infarct. A chest x-ray film was normal (the heart was of normal size and configuration). The patient stated that she would like to have visitors but felt embarrassed when she could not remember who the visitors were. Four weeks after the heart attack, results of bromsulphalein, phenosulfonphthalein, and cephalin-flocculation tests were all negative. The following week her memory was improving, and she could remember the names of her husband's five sisters. At that time she was fitted with a foot brace; before that she had had physiotherapy and other measures to bring back the strength in those

paralyzed muscles. An electrocardiogram on June 2 indicated healed or healing posterior infarct.

Six weeks after admission she was able to walk alone. After seven weeks she had no complaints, played all the nursery rhymes on the piano at home, but still had difficulty remembering names of people. Two months after her heart attack she was doing her own cleaning and housework. By three months after, she was getting movement in her left foot and was able to bring the foot up to a 90° angle with the leg. At that time she was able to discard the brace. She now has returned to her bridge club, and although she still has trouble remembering names she has no trouble playing bridge.

Summary

This was a case of a 55-year-old woman who had an acute myocardial infarct and either cardiac arrest or ventricular fibrillation and who was treated successfully in the home by means of external cardiac massage and mouth-to-mouth respiration. The important factors in this case which led to a successful resuscitation were thought to have been: (1) the insult being such that resuscitative measures were able to restore the partially wounded heart to beat again; (2) the promptness of treatment; (3) the presence of two persons trained in resuscitation; (4) the availability of nasal oxygen; (5) the use of an emergency airway; (6) the positioning of the patient with the head back and the legs elevated; (7) the early administration of Aramine; and (8) the continued attention in the hospital.

Patient and Doctor

When I was ill you came to me,
 Doctor, and with great urgency
 A hundred students brought with you
 A most instructive case to view.
 The hundred fingered me with hands
 Chilled by the blasts from northern lands!
 Fever at outset had I none;
 I have it, sir, now you have done!

Martial (43-102)

By a blessed dispensation, human beings forget physical pain much more quickly than they do their joyous emotions and experiences. A merciful Providence passes the sponge of oblivion across much that is suffered, and enables us to cherish the great moments of life and honour which come to us in our march.

— Winston Churchill, 1949

WHAT'S YOUR DIAGNOSIS?

A 35-year-old white female had been ill for approximately one week. On the second day of the illness, she had taken to her bed because of increasing weakness.

Her unsuccessful husband had not called a physician since there was no physician to call. Had a physician visited the patient, he would have found her in a rough, unfinished log cabin at Pigeon Creek, Indiana. He would have seen that her sick bed was a crude affair of poles stuck between the logs in a corner of the cabin, and that the cabin floor was dirt.

In taking the history, the physician would have learned that the patient loved milk and that one of the family's milk cows had died recently of the trembles. (These twin facts might or might not have impressed him as significant.) In inventorying the symptoms, he would have found that the patient had been ill for about a week with nausea, vomiting which was becoming increasingly intractable, malaise, obstipation, and an increasingly foul breath.

In the absence of a physician, the family cared for the patient as best they could. From her bed the sufferer could look out the door (for there were no windows) and see the riotously beautiful foliage in that autumn of 1818. Sick though she was, she must have enjoyed the panoply of colors — her last pleasure in a pitifully somber life.

Now, with a week gone by, she was becoming weaker and weaker. Feeling her life slipping away, she marshalled her waning strength and called her nine-year-old son to her. Fumbling with the boy's head as if to bless him, she told him in broken tones that he must always do right and be good to his sister and to his father.

A few more days and the patient was dead; she was borne in a rough-hewn cherry coffin to a wooded knoll about a quarter of a mile from the house and buried near the fresh graves of Mrs. Brooner, a neighbor, and Betsy and Thomas Sparrow, the patient's aunt and uncle — all of whom had died recently of the same ailment.

What is your diagnosis? Turn to page 495.

Pioneer Doctor's Fees

Charges for medical services varied. Dr. Drake said that the ordinary charge was 25 cents a mile, 'one half being deducted and the other paid in provender for his horse, or produce for his family.' In the earlier years the average country doctor would probably settle for 25 to 50 cents for a local visit, or a dollar if he sat up all night. The Indiana law of 1816 fixed fees at 12½ cents per mile of travel by day, double by night, but these fees were not strictly adhered to. Springfield, Illinois, physicians, for instance, agreed in 1840 to the following scale: daytime visit in town, \$1; up to four miles, \$2; each additional mile, 50 cents; prices double for night visits; verbal advice, \$1; each dose of medicine, 50 cents; vaccination, \$1; natural parturition, \$5 to \$10; fractures, \$5 to \$10; amputation of leg or arm, \$25 to \$100; lithotomy, \$100 to \$200.*

*Pickard and Buley: *The Midwest Pioneer*, Henry Schuman, New York, 1946.

Duodenal Atresia and Maternal Hydramnios*

LOWELL W. BARR, M.D.
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ATRESIA** of the duodenum implies a lack of continuity at this level in the gastrointestinal tract. It is to be distinguished from stenosis in which there is a narrowing or stricture of the lumen. Duodenal atresia is a rare congenital condition which occurs once in 20,000 to 30,000 births. Obstruction may also be manifested by congenital diaphragms or multiple segments of stenosis. All of these defects develop during the sixth week stage of the embryo and are explained by a failure of the vacuolization and coalescence process that occurs in the solid cord state of this portion of the gut.¹ Duodenal atresia may be associated with atresia in other parts of the alimentary tract and with other developmental imperfections, such as harelip and cleft palate. A significant number of subjects with duodenal atresia are found to have Downs syndrome² or cystic fibrosis.³

Utero Signs

Hydramnios is an excessive quantity of amniotic fluid — usually over 1200-1500 cc. According to Ehrlich,⁴ who discussed the mechanism of hydramnios in duodenal atresia, a fetus normally begins to swallow amniotic fluid at the time kidney function starts, near the end of the fourth fetal month. If the swallowing act is delayed or absent, the fluid in the amniotic sac may be increased, leading to hydramnios. Such a delay also occurs in high obstruction of the alimentary tract, in which case the resorption of the amniotic fluid is missing. There is a definite correlation between hydramnios and congenital fetal malformations in which either the normal intrauterine deglutition or intestinal resorption is disturbed. These malformations include atresias and extrinsic or intrinsic obstructions of the upper alimentary tract. In fifty per cent of

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**See Test Your Word Score Page 521.

the patients who develop hydramnios in the last trimester of an otherwise normal pregnancy, a fetal anomaly will be responsible for the hydramnios.⁵

Signs, Symptoms and Diagnostic Tests

The signs and symptoms of atresia are those of complete high intestinal obstruction. Vomiting begins soon after birth and



Fig. 1 — X-ray of Case 2 after giving gastrograffin by mouth. The greatly dilated duodenum appears as a round ball on the patient's right side.



Fig. 2 — Case 2. The dilated duodenum and the dilated stomach, separated by the pylorus, present an hour-glass appearance.

is persistent. Often large amounts of fluid may be obtained if the stomach is emptied by naso-gastric tube. Bile is usually seen but may be absent in the vomitus if the atresia occurs proximal to the ampulla of Vater. Abdominal distention, when present, is confined to the stomach and upper duodenum. Peristaltic waves may be seen traversing from left to right across the epigastrium. Stools may be absent or scant, dry and white.

Cornified epithelial cells which are desquamated from the skin of the fetus and swallowed with the amniotic fluid are present in normal meconium. The absence of these cells in the stool is presumptive evidence of intestinal or colonic obstruction. The stool specimen is smeared on a glass slide, stained with gentian violet and decolorized. The dye is removed from all cells except the cornified epithelial cells. This is known as Farber's test.⁶

The plain x-ray film of the abdomen is the most useful diagnostic aid. Air in the distended stomach and duodenum produces the "double bubble" or "hour-glass" effect, with absence of air in the intestine and colon. If a thin barium mixture or gastrograffin is instilled into the stomach, x-ray examination will reveal the greatly distended stomach and duodenum, with complete obstruction of the duodenum.

Surgical Treatment

Preoperative preparation and postoperative care form the cornerstone of treatment for these babies. The isolette provides a protective environment to permit adequate control of temperature, humidity and oxygen and allows adequate observation in the nursery. Suctioning and resuscitating equipment designed for infants should be readily available. Careful management of intravenous fluids and electrolytes requires well calibrated infusion sets. Intravenous fluids can be given by cut-down or by using small scalp vein sets; but because of the possibility of the late complication of extrahepatic portal-vein obstruction and portal hypertension, the umbilical vein should be avoided. Administration of fluids to newborns should be constantly monitored by the physician,

who should be alert to signs of over-hydration — puffy face or feet, tachypnea and tachycardia. Edema of prematurity must be taken into consideration and weighed against other evidence of over-hydration.

A basic solution of one part normal saline to four parts of 10% dextrose covers most needs of the newborn. Normal saline should be added to cover for gastric fluid lost by suction or vomiting. A safe amount of fluid in the first few days of life can be supplied by administering 50-60 ml./kg./24 hours if the baby is not dehydrated. By the fifth day the fluid requirement may total 100-150 ml./kg./24 hours.⁷

Prematures or infants may maintain water balance with as little as half these amounts if kept in high humidity. Sodium bicarbonate and potassium should be added, depending upon clinical findings and serum levels.

Blood should be typed and cross-matched for replacement during surgery, with a gastric tube in place during the operative procedure. General endotracheal anesthesia may be used, but local anesthesia may be satisfactory, especially in small or debilitated infants.

An anastomotic procedure to circumvent the atretic area is indicated. Duodeno-duodenostomy is the operation of choice, but gastrojejunostomy is satisfactory and is mandatory when the atresia involves the first portion of the duodenum. The entire length of the small bowel and colon should be examined for other areas of atresia.

Case Reports

Case 1

A 5-pound, 13-ounce boy was born to a twenty-seven-year-old woman as her eighth child on March 28, 1954. Moderate hydramnios was noted. The baby regurgitated all feedings but had small meconium stools. The vomitus was clear. The weight dropped to 4 pounds, 10½ ounces. Physical examination was negative except for dehydration and distention of the upper abdomen. Radiograph of the abdomen revealed a distended stomach and absence of air in the bowel.

On April 1, under local anesthesia, an upper right rectus incision was made. The stomach was tremendously dilated, the dilatation stopping abruptly at the duodenum which was atresic for a distance of about one centimeter. The cecum was adherent to the greater curvature of the stomach indicating incomplete rotation of the bowel. A



Fig. 3 — Case 3. X-ray of the abdomen made within an hour after birth. There is a bubble of air in the duodenum and a slightly larger bubble in the stomach. This is probably the earliest x-ray of the abdomen ever made in a patient with duodenal atresia.



Fig. 4 — Case 3. X-ray of abdomen made eight hours after birth. The characteristic "double bubble" sign is well demonstrated.

retrocolic gastrojejunostomy was performed. At the completion of the anastomosis the small bowel was distended by the gas which rushed into it.

Fluids and blood were administered through a cut-down, and feedings were begun cautiously on the third postoperative day. The patient did well and was discharged in four weeks, weighing 6 pounds, 3¼ ounces. He is now 12 years old and is normal in all respects.

Case 2

A woman, age 36 years, was admitted to the hospital on November 27, 1964, in strong labor. Previously she had had two Cesarean sections and an operation for tubal pregnancy. Under spinal anesthesia a low cervical Cesarean section was done and a 3-pound, 2½-ounce male infant was delivered. Hydramnios was noted. In spite of its small size, the infant cried at once and seemed quite vigorous, and the Apgar score was 10. Rales were heard in both lungs. The baby's stomach was aspirated and 45 cc. of fluid removed. No feedings were given by mouth and repeated aspirations were carried out.

On the second day antibiotics and intravenous fluids were started. X-ray of the abdomen revealed a moderate amount of gas in the stomach but absence of gas in the bowel distal to the duodenum. A gastrointestinal study with "gastrografin" revealed complete obstruction of the duodenum.

With a preoperative diagnosis of duodenal obstruction, operation was carried out the second day under local anesthesia. The stomach and first portion of the duodenum were greatly dilated, and beyond this area was a segment of atresia. A duodeno-duodenostomy was performed and the operation well tolerated. Bowel sounds were active on the day following operation and feedings of small quantities (10 cc. every two hours) were started. On the fifth day the patient had several stools. Feedings were increased and were retained. On December 5 the baby was tolerating feedings, and there were active bowel sounds. Feedings were then increased, and on the tenth postoperative day full strength feedings were given. However, the rales in the chest persisted. Respiratory distress slowly increased and an x-ray of the chest showed heavy bilateral bronchopneumonia. The baby's condition gradually deteriorated and he expired on the fourteenth postoperative day. At post mortem, the duodeno-duodenostomy was functioning well. There was severe bilateral bronchopneumonia. The cause of the pulmonary disease was comparable to that seen in some infants with cystic fibrosis.

Case 3

On July 10, 1965, a 5-pound, 8-ounce male baby was born to a 45-year-old woman as her fourth child. The delivery was vaginal, and hydramnios, estimated to be over 3000 cc., was present. The baby breathed spontaneously but appeared to be mongoloid. The Apgar score was 10. Soon after birth the baby spit up amniotic fluid, and repeated gastric aspirations yielded 30-35 cc. of bile-stained fluid. X-rays of the abdomen at one hour and at eight hours of age showed the typical double bubble of duodenal atresia. A barium enema

showed a normal colon. Surgery was done under local anesthesia at 18 hours of age. The stomach and first portion of the duodenum were greatly dilated; the jejunum and ileum were empty. A duodeno-duodenostomy was carried out. X-rays taken on the fourth day showed a passage of gas through the anastomosis, and the baby tolerated feedings. With apparently normal gastrointestinal function the baby has done well.

Discussion

Surgery offers the only hope of survival and should always be done. Although, Ernst⁸ performed the first successful operation for relief of duodenal atresia in 1914, many years elapsed before there were reports of other successful attempts. In 1931 Webb and Wangenstein⁹ stated that there had been only nine operative triumphs up to that time and that their two efforts had ended in failure. Nevertheless, successful management of an infant with atresia of the second portion of the duodenum associated with complete biliary obstruction was not reported until 1960.¹⁰ Not until 1953 did Gross¹¹ report on the operative treatment of thirty-two cases.

Glover and Barry,¹² in 1949, reported a mortality of 75% in the treatment of patients with complete intestinal obstruction. According to Evans,¹³ prior to 1951, only 139 patients with intestinal atresia had been successfully treated and reported. More recently Gross¹¹ reported a mortality of 50% in patients with duodenal atresia. In a 1963 symposium Dr. Tague Chisholm¹⁴ commented on the survival of infants with intestinal obstruction requiring surgery: "of term infants with no other major anomalies, three fourths are surviving today with present management, whereas, 20 years ago, three fourths of these infants died; but with premature or term babies who have associated serious anomalies, the record is rather disheartening — with only about 25 percent surviving." The causes of mortality are associated anomalies, prematurity, delayed operation, inadequate supportive therapy, operative indecision, cystic fibrosis and chest complications.

Summary

1. Duodenal atresia is a rare congenital

condition which occurs once in 20,000 to 30,000 births.

2. Hydramnios is a frequent accompaniment of duodenal atresia and its presence should arouse suspicion of an obstructed duodenum.

3. Surgery offers the only prospect of cure. A circumventing procedure, preferably a duodeno-duodenostomy, is indicated and should be attempted in all cases.

4. Early diagnosis, preoperative and post-

operative care are the cornerstones of successful treatment.

5. The mortality following operative treatment fluctuates between 25% and 75%. Prematurity, associated anomalies, and chest complications contribute to the mortality.

6. Mongolism is present in 20-30 percent of cases of duodenal atresia.

7. Cystic fibrosis is present in one fourth of cases of duodenal atresia.

8. Three cases of duodenal atresia with maternal hydramnios are presented.

References

1. Harberg, F. J. and Biggs, T. M.: Congenital Duodenal Obstruction. *Amer Surg* 29:506, 1963.
2. Darby, R. E. and Melamed, A.: Duodenal Obstruction with Mongolism. *Wisconsin Med J* 63:282, 1964.
3. Anderson, D. H.: Pathology of Cystic Fibrosis. *Ann N Y Acad Sci* 93:500, 1962.
4. Ehrlich, A. W.: Significance of Hydramnios in Diagnosis of High Congenital Obstruction of the Alimentary Tract. *Ann Pediat* 199:596, 1962.
5. Lloyd, J. R. and Clatworthy, H. W. Jr.: Hydramnios as an Aid to the Early Diagnosis of Congenital Obstruction of the Alimentary Tract: A Study of the Maternal and Fetal Factors. *Pediatrics* 21:903, 1958.
6. Farber, S.: Congenital Atresia of Alimentary Tract Diagnosed by Microscopic Examination of Meconium. *JAMA* 100:1753, 1933.
7. Wetton, R.: Fluid Therapy in the Newborn Infant. *Pediat Clin N Amer* 11:4:1019, 1964.
8. Ernst, N. P.: A Case of Congenital Atresia of the Duodenum Treated Successfully by Operation. *Brit Med J* 1:644, 1916.
9. Webb, C. H. and Wangenstein, O. H.: Congenital Intestinal Atresia. *Amer J Dis Child* 41:262, 1931.
10. MacKenzie, W. C., Long, A., Friedman, M. H., and Calder, J.: Congenital Atresia of the Second Portion of the Duodenum with Associated Obstruction of the Biliary Tract. *Surg Gynec Obstet* 110:775, 1960.
11. Gross, R. E.: The Surgery of Infancy and Childhood, 150-166, W. B. Saunders, Co., Philadelphia, 1953.
12. Glover, D. M. and Barry, F. M.: Intestinal Obstruction in the Newborn. *Amer Surg* 130:480, 1949.
13. Evans, C. H.: Atresia of the Gastrointestinal Tract. *Surg Gynec Obstet Inter Abstr Surg* 92:1, 1951.
14. Chisholm, T.: Problems in Neonatal Surgery (Ross Laboratory Conference), p. 71, October, 1963.

ANSWER TO WHAT'S YOUR DIAGNOSIS (From page 490).

The patient was Nancy Hanks Lincoln — Abraham Lincoln's mother. The cause of her death was milk sickness.

Unfortunately, the general tendency of things is to render mediocrity the ascendant power. At present, individuals are lost in the crowd, and it is almost a triviality to say that public opinion now rules the world. And public opinion is the opinion of collective mediocrity and is expressed by mediocre men. The initiation of all wise and noble opinions must come from individuals, and the individuality of those who stand on the higher eminences of thought is necessary to correct the tendency that makes mankind acquiesce in customary opinions.

— John Stuart Mill

In your relations with people it is necessary to try to give them as much as possible and to take from them as little as possible. — Tolstoy

Dr. John Richmond

In Newton, Ohio, in 1827, Dr. John Richmond performed the first recorded Caesarean section west of the Alleghenies. Some idea of the magnitude of his task might be obtained from his own report:

"I had no recourse to cordials, for these could not be obtained. I was seven miles from home, and had but few medicines with me. . . . I requested advice, which, however, could not be obtained, on account of high water in the Little Miami and the darkness of night. . . . After doing all in my power for her preservation, and feeling myself entirely in the dark as to her situation, and finding that whatever was done, must be done soon, and feeling a deep and solemn sense of my responsibility, with only a case of common pocket instruments, about one o'clock at night, I commenced the Caesarean Section. . . . The night was stormy and windy, insomuch, that the assistants had to hold blankets to keep the candles from being blown out. Under these circumstances it is hard to conceive of the state of my feelings, when I was convinced that the patient must die, or the operation be performed. . . . The patient never complained of pain during the whole course of the cure. She commenced work in twenty-four days from the operation, and in the fifth week walked a mile and back the same day."*

*Pickard and Buley: *The Midwest Pioneer*, Henry Schuman, New York, 1946.

Laughter

"Why is laughter so pleasant?" asked someone.

"Because," someone answered, "laughter relieves us of superfluous energy, which, if it remained unused, might become negative, that is, poison. We always have plenty of this poison in us. Laughter is the antidote. But this antidote is necessary only so long as we are unable to use all the energy for useful work. It is said of Christ that he never laughed. And indeed you will find in the Gospels no indication or mention of the fact that at any time Christ laughed.

"But there are different ways of *not* laughing. There are people who do not laugh because they are completely immersed in negative emotions, in malice, in fear, in hatred, in suspicion. And there may be others who do not laugh because they cannot have negative emotions. Understand one thing. In the higher centers there can be no laughter, because in higher centers there is no division, and no 'yes' and 'no.' "

— P. D. Ouspensky

Derivatively Speaking

Symptom — from Greek *symptoma* (anything that has befallen one)

Regional Circulation in the Brain Using a Scintillation (Anger) Camera

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DYNAMIC STUDIES of isotope distribution in the body are at present being made possible by the use of gamma camera instruments. This report summarizes some preliminary trials with a scintillation (Anger) camera|| which is being used to study the distribution of blood within the human brain. The ultimate aim of the present study is to develop a method by which data on regional cerebral circulation may be accumulated in a rapid fashion in order to diagnose localized abnormalities of blood flow to the brain.

Principle

The clearance techniques as previously reported for studying the regional cerebral blood flow are based upon a recording of the wash-out curve of a freely diffusible isotope over a period of 10 to 15 minutes. The clearance curve is then a function of the blood flow.^{1,2} In the present study we have utilized a modification of the bolus fractionation technique of Sapirstein.³ This technique assumes that blood going to the brain is suddenly labelled at a uniform concentration with an indicator which is quantitatively retained at the tissue level, such that each tissue component will accumulate radioactivity in proportion to its blood flow. Pre-supposing iso-efficiency counting, the differences in externally measured radioactivity will be proportional to differences in blood flow. This means that the gamma camera will "see" areas of different intensity of radioisotopic pickup which will then be directly proportional to the blood flow to the different parts of the organ visualized

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||Nuclear Chicago.

on the two-dimensional display of this instrument. It is possible to combine this use of the "bolus fractionation" technique with the above mentioned isotope clearance technique, i.e., to record radioactivity during the clearance phase and from these data determine regional blood flow in quantitative terms of ml/g/min.

The Tracer

Bolus-Fractionation Technique

The principle involved in the bolus-fractionation technique is perhaps best conceptualized by considering the use of a radioactive macrocolloid injection at the aortic root. If the extraction of the isotope from the blood is 100 per cent during the first passage through the peripheral vascular bed, then clearly the isotope uptake in the different organs will correspond to the distribution of blood flow. As the retention of a macroaggregated tracer such as 99m technetium albumin is of hours' duration, instruments requiring considerable time for image formation, e.g., scanners, can be used effectively for obtaining high resolution scintiphotograms. This technique is presently being used to good advantage for studying pulmonary circulation in numerous radioisotope clinics. Due to the possible risks of ischemic tissue damage in the brain this type of indicator is in principle less attractive than a freely diffusible inert radioactive gas such as 133-xenon.^{4,5}

Diffusible Inert Indicators

Freely diffusible inert indicators move rapidly out of the capillaries, depending upon concentration differences between the blood and surrounding tissues. The initial extraction from the blood of these indicators into the tissue during the first capillary passage is therefore very high, approaching 100 per cent, since diffusion equilibrium is believed to occur in less than one second.⁶

*It is not possible to use hydrophilic radioactive ions such as 42-K or 86-Rb for brain blood flow studies since the blood brain barrier is normally almost impermeable to crystalloids.⁷ (This is mentioned here since for other organs, such tracers might be used in accordance with the Sapienstein principle under discussion.)

**Since this instrument can record only a single emission event at any one instant, there is an interval, albeit in the micro-second range, between each recorded emission. This interval is called the "dead-time."

These lipophilic freely diffusible tracers* are of two types:

NON-VOLATILE: Iodo-antipyrine is the most widely used indicator of this type.

VOLATILE INDICATORS: The extremely short biological half-life of inert gases such as 85-Kr or 133-Xe makes it possible to administer rather large quantities of radioactivity to patients without significant radiation hazard. Calculation shows that an intravenous or intra-arterial injection of 40 millicuries of xenon-133 dissolved in saline results in a gonadal dose of about 10 millirads — which is about 2 per cent of the gonadal dose from an ordinary x-ray film over the pelvis and a level considered safe for routine diagnostic isotope work.* Such doses of these radioisotopes would result in counting rates which are considerably higher than can optimally be recorded by any gamma camera device available at the present time. It is concluded therefore that, in practice, the upper limit for the activity of 133-xenon used is governed more by the resolving characteristics of the instruments used than by the radiation dose to patients.

Radioactive Gas

Of the many radioactive gases which exist, 133-xenon appears at present to be the most promising. It is readily available and has a half-life of 5.27 days and a gamma emission of 81 Kev. which is suitable for localization studies with instruments presently available. This is particularly true for our scintillation camera in which bialkali cathode phototubes have been installed. The lower work function for electron release in these phototubes permits improved resolution in studies employing radioisotopes such as 133-xenon which emits relatively low energy gamma photons.

With the use of 5-10 millicuries of 133-xenon, very high counting rates are to be expected, so that the "dead-time"*** of the recording instrument should be maintained at an absolute minimum. Recent circuitry modifications have decreased the dead-time for our scintillation camera to about 4 microseconds which appears to be about

the best obtainable with an instrument of this design but sufficiently good to permit pictures of isotope distribution to be obtained at intervals approaching one second.

Intra-Arterial Injection of 133-Xenon

By slug injection of 133-xenon dissolved in saline via the internal carotid artery only the brain receives the radioactive indicator. This is obviously a major advantage over a common carotid artery or other injection in which the radioisotope may be taken up in other tissues. Slug injection refers to the administration of a small amount of the radioisotope solution, about 2-5 milliliters, in about one second. This rapid injection implies that the period during which the isotope distribution is a function of flow is very short, being in the order of about 8-10 seconds. Following this time the initial high uptake of 133-xenon in high flow regions will decrease due to wash-out by non-labelled blood. The briefness of such a study necessitates that a relatively large dose of 133-xenon, about 10 millicuries, must be used in order to accumulate enough counts during the 0.1-0.3 minutes available for several serial photographs to be taken.

Internal Carotid Artery Injection of 10 Millicuries of 133-Xenon

A 67-year-old patient, with hemiparesis secondary to a stroke syndrome, received an injection of 10 millicuries of radioactive xenon gas dissolved in saline. This study was performed before high speed circuitry was added to our gamma camera so that it is very evident from the pictures obtained that the resolution was very poor, due to overloading. Figure 1 is the first picture in a series obtained and demonstrates the passage of the bolus up the carotid artery. It is readily appreciated that this picture demonstrates much less resolution than obtained from an "arterial phase arteriogram" which ideally might be expected and indicates the need for improvement in resolution of gamma camera systems.

Prolonged injection at a constant rate (or perhaps with a slightly increasing speed over 0.5 to 1.0 minutes) solves the difficulty of the very brief "filling-up" period but does

not provide clearance data from which cerebral blood flow may be calculated.

Common Carotid Artery Injection of 4 Millicuries 133-Xenon

Injections into the common carotid artery can also be made according to both methods referred to above, i.e., with the bolus technique or with a prolonged injection. However, this leads to substantial "contamina-



Fig. 1 — This scintiphotogram was obtained during the first 5 seconds after the administration of 10 mc. of 133-xenon in saline via catheter in the right internal carotid artery. This right lateral projection shows gross distribution of the radioactivity extending from the internal carotid artery throughout the right hemisphere.



Fig. 2 — This right lateral scintiphotogram was obtained immediately following the administration of 4 mc. of 133-xenon in saline via the common carotid artery. Exposure time was 10 seconds. The radioactivity is seen to be present in structures perfused by the external carotid artery as well as that part of the brain perfused by the internal carotid artery. It may be noted that there is very little uptake in the posterior fossa.

tion" of the picture by the ^{133}Xe arriving into the field via the external carotid artery⁹ (Figure 2). The patient for this study was a 62-year-old man with left hemiparesis and confusion. Injection of the isotope into the common carotid artery showed highly blurred pictures due to large amounts of isotope in the face area and the



Fig. 3 — This scintiphotogram was obtained using 4 mc. of ^{133}Xe in saline injected into the right common carotid artery. This is a right lateral view with an exposure time of 20 seconds. A lead shield was placed over the face. There is an area of decreased intensity in the centro-parietal region which corresponds to a slow wave EEG focus and to what was thought clinically to be an area of infarction. Another scintiphotogram obtained later in the series failed to show this area of decreased intensity.

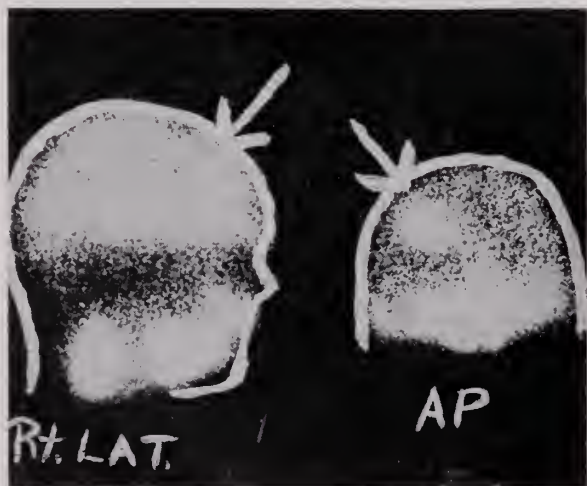


Fig. 4 — These scintiphotograms of the right lateral and anterior projections of a patient were obtained two hours after the intravenous administration of 10 mc. of $^{99\text{m}}\text{Tc}$ (pertechnetate). There is a focus of radioactivity in the right frontal area (shown by arrows) which represents metastatic spread of a breast carcinoma.

air ways. Of interest is the absence of counts in the posterior neck region not supplied by the common carotid artery.

This study was repeated with a lead shield over the face. The resolution was better, and there is a small area of relatively few counts in the midportion of the hemisphere where large numbers of counts should be expected (Figure 3). This likely represents an ischemic lesion corresponding to the patient's symptoms and the focal abnormality in an EEG tracing.

Inhalation or Intravenous Injection of ^{133}Xe

For ^{133}Xe inhalation studies the patient breathes from a spirometer containing about 5 liters to which 5-10 millicuries of the radioactive gas has been added. A lead shield is used over the facial structures as has been described for common carotid artery injections. A blood pressure cuff has also been used around the base of the skull to eliminate "contamination" from radioactivity via the extracerebral arteries.

Inhalation of ^{133}Xe

The patient was a 40-year-old woman with a metastatic brain tumor in the right frontal region as seen by a $^{99\text{m}}\text{Tc}$ study (Figure 4). During the initial portion of the inhalation period of four minutes, a definite region of low uptake could be seen which appeared to correspond to the location of the tumor (Figure 5). This regional uptake difference was not appreciated on later pictures and demonstrates how the isotope distribution changes during the clearance phase. Thus the initial regional differences in perfusion observed during the bolus fractionation period tend to be lost.

Intravenous Administration of ^{133}Xe

After an intravenous injection, the isotope must first pass through the lungs before reaching the brain. Since much activity will be lost in this process, solutions of relatively high activity must be used. Except for this fact, the intravenous study would be essentially identical to the inhalation study without the complication of a spirometer, mouth piece, etc. From a general

clinical standpoint the intravenous administration would seem to offer an attractive alternative to the inhalation route.

The patient in this study was a 65-year-old man with a cerebral hemorrhage followed by complete aphasia and right-sided hemiplegia. The gamma camera pictures following administration intravenously of 10 millicuries of ^{133}Xe in 5 milliliters saline showed just a bare suggestion of radioisotope uptake in the left hemisphere (the parieto-occipital area). The initial pictures in this series showed minimal uptake in the airways which are always clearly visualized on the inhalation studies. This indicates another potential advantage of intravenous administration of ^{133}Xe over its being inhaled.

Administration of Iodoantipyrine

One patient in our series received an intravenous injection of 1.5 millicuries of ^{131}I -iodoantipyrine. This study revealed that this indicator is not suitable for cerebral circulation studies with the scintillation camera. The scintiphotograms of the head of this patient were extremely blurred and no contours of concentration differences could be discerned.

Discussion

Results of studies shown in the last section indicate the limitations of the scintillation camera for pictorial representation of regional cerebral blood flow. Two improvements were made during the course of these studies which have significantly improved the resolution of this system. The first of these was the insertion of bialkali phototubes with lower work functions than photo multiplier tubes heretofore available. This has meant greater efficiency in the detection of relatively low energy gamma rays as well as better correlation between the position of the scintillation event in the crystal and its position on the scintiphotogram. A second important improvement has been the modification of the electronics to permit a more rapid accumulation of data. Consideration is now being given to changes in collimator design and possibly the use of

a thinner crystal, particularly for low energy gamma emitters.

Carotid Isotope Injections

In general, carotid isotope injection studies are hampered in their interpretation by the fact that one can never be sure, without angiographic studies, what areas an individual artery will supply. A region of low uptake will not necessarily mean a region of low blood flow. It could represent a region supplied by an artery other than the one injected. An extreme example would be that of a thrombosis of the common carotid artery on one side. With adequate collaterals from the vertebrals and other vessels, the area normally supplied by the occluded vessel may have normal blood flow despite the fact that no ^{133}Xe can be deposited intracranially following injection into the carotid artery proximal to its occlusion. Flow in this case could be explored by injecting the isotope into one of the vessels supplying the collateral flow, for example, the contralateral carotid artery. This technique will then offer an approach to evaluating the effect of carotid occlusive lesion.

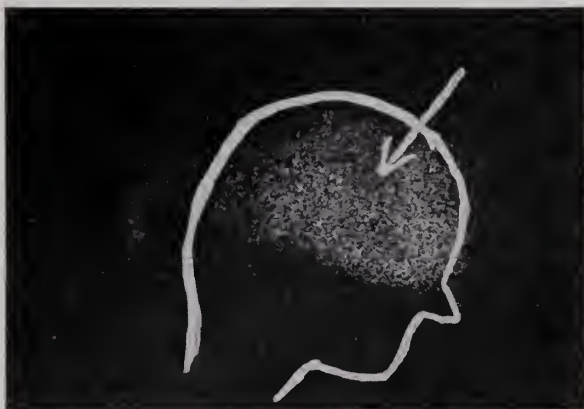


Fig. 5 — This right lateral scintiphotogram was obtained using ^{133}Xe administered to the same patient whose brain study is shown in Figure 4. The ^{133}Xe was administered by inhalation from a spirometer containing approximately 10 mc. of xenon in 5 liters of air. A lead shield was used to eliminate the pick-up of radioactivity from the muscles of the face and other areas perfused by the external carotid artery. This scintiphotogram gives the impression of a decreased uptake of ^{133}Xe in the area of the metastatic lesion. Right lateral scintiphotograms obtained later in the course of inhalation of the ^{133}Xe and also during its clearance phase did not show this apparent decrease in activity in the region of the metastatic lesion.

Some improvement in the common carotid injection technique is derived by the use of a suitable blood pressure cuff applied around the skull during the injection phase of the study. By inflating this cuff above systolic pressure, "contamination" of the gamma camera picture by radioactivity in tissues perfused by the external carotid arteries is significantly reduced.

The initial pathophysiological process in apoplexy is undoubtedly localized ischemia, i.e., local deficiency of blood flow. In such an area one must expect to find an absence or a diminution of isotope uptake when the isotope is administered in one of the ways described above. However, we know that these localized areas of ischemia often lie deep within the cerebral hemisphere so that other projections, e.g., coronal, may be desirable in order to graphically demonstrate the ischemic focus.

Vascular Brain Lesion

In this context it should be pointed out that a localized vascular lesion in the brain will affect the whole brain rather markedly. Regional measurements of cerebral blood flow in typical focal vascular cerebral disorders have usually shown a general decrease of the blood flow, not only in the area of infarction, but also in areas which are clinically and angiographically normal.¹⁰ This "remote" effect of the focal lesion will, in studies of the present type with the gamma camera, lead to a diminished contrast between the lesion and the normal surrounding brain.

Ischemic Focal Lesion

In an ischemic focal lesion the diminished focal flow may not persist, since the underlying obstacle for the blood flow may be relieved by an increase in perfusion pressure, by lysis of an embolus, or by the take-over of collaterals. The flow may return to normal or nearly so within the lesion even if the localized symptoms persist because of cellular damage. It is even quite likely that, in part, a hyperemia may develop due to the uncoupling of the normal vasoconstrictor tone of the cerebral vessels. There is some angiographic evidence for such a hyperemic

zone around local vascular insufficiency areas in the brain.¹¹ This hyperemic zone would, naturally, show up in isotope studies of the present type as areas of increased uptake.

It should also be pointed out that, in principle, it is much more difficult to record a "negative" picture than one that is positive. A study of the present type which aims at picturing differences and abnormalities in blood flow yields a negative shadow and should therefore be correlated when possible with "positive" scintiphotograms obtained following administration of 99m technetium or 197 mercury chlormerodrin to patients suffering from vascular lesions causing cerebral infarction.

Inhalation Approach

Our experience thus far indicates that the inhalation approach to administration of 133-xenon for cerebral blood flow studies shows considerable promise. For these inhalation studies approximately 5 to 10 mc. of 133-xenon is placed into a spirometer system. The patient breathes the xenon-air mixture from this system which is so arranged that oxygen is added to compensate for the carbon dioxide which is continuously removed. The time of breathing in this manner is usually restricted to three minutes in order to maintain a small radiation dose to the patient. This is usually sufficient time for the xenon to reach equilibrium in the patient. In individuals with some form of pulmonary disease, we find that the equilibrium has not been reached in this time and consideration is being given to longer breathing times for these patients. The effect, if any, of the spirometer breathing time *per se* on the clearance curves is being investigated. A lead shield is being used over the facial structures to mask out xenon activity in extracranial tissues, as was described for common carotid artery injections. An inflatable cuff is being used around the base of the skull to eliminate, insofar as possible, "contamination" from radioactivity arriving via the extracerebral arteries. A lead shield is also being used to eliminate xenon activity in respiratory passage ways as well as other extracranial tissues.

During the clearance period which follows the uptake, there is a redistribution of the radioisotope as it clears body tissues. This complicates the analyses of curves relating to xenon clearance from the brain, particularly in individuals with pulmonary disease. Our present protocol for evaluation of cerebral blood flow following inhalation of 133-xenon therefore includes corrections for clearance of 133-xenon from extracerebral tissues and for the small percentage of 133-xenon which is not cleared in one passage through the lungs and thus returns to the systemic circulation.

Results

The results of our single study with iodoantipyrine left much to be desired. The reasons for the poor success in this particular study are: (1) The 364 Kev. photopeak of 131-iodine is well above the energy range for which the scintillation crystal is most efficient. (2) The complex spectrum of 131-iodine, which includes high energy components and consequently contributes to significant scatter. (3) The level of radioactivity in the brain remains low. A total count recorded over the first 15 seconds was only 2500, which was much too low to permit adequate resolution on a scintiphogram. It is concluded from the study with iodoantipyrine that one would need to use on the order of 200 millicuries of this radioisotope to obtain reasonably good pictures. Such high doses cannot be used routinely due to the long effective half-life and hence radiation hazard of the isotope in question.

Considerations for Improvement

Our ultimate aim is to be able to quantitate regional cerebral blood flow. As an initial step in this direction, we have modified

our scintillation camera to permit graphic recording of data from each data of radioactive uptake and clearance from each cerebral hemisphere. Our next step will be to utilize computer analyses of the curves obtained in this way.

An obvious extension of this would be to obtain curves representative of regional cerebral blood flow. We are contemplating the use of automatic time lapse photography with a movie camera to record in sequence the changing pattern of radioactivity as displayed by the cathode ray tube read out of the scintillation camera. The serial pictures obtained in this way should permit a qualitative analysis of total and regional cerebral blood flow. A flying spot scanner might be used to analyze the distribution of radioactivity on the time lapse pictures obtained in such a way that computer analysis of the data obtained might be contemplated. An alternative plan which is being considered is to utilize video tape to record the changing pattern of radioactivity as seen on the oscilloscope read out. This tape might then be played back through a television system and an analysis made of any desired cross-sectional areas as represented on the television screen. The data obtained in this way may again be processed for computer analysis.

Once the techniques have been established we are hopeful of studying routinely all stroke or potential stroke patients. The effect of vasodilators, etc., on cerebral blood flow will be investigated. In this way each patient may serve as his own control. Patients will also be studied before and after surgical correction of arterial occlusions to better evaluate changes in cerebral blood flow related to the surgical procedure.

References

1. McHenry, L. C.: Cerebral Blood Flow. New Engl J Med 274:82, 1966.
2. Lassen, N. A., Ingvar, D. H.: Regional Cerebral Blood Flow Measurement in Man: Review. Arch Neurol 9:615, 1963.
3. Sapirstein, L. A.: Measurement of Cephalic and Cerebral Blood Flow Fractions of the Cardiac Output in Man. J Clin Invest 41:1429, 1962.

4-11 May be secured from the author or the reprints.

Whence?

Do we bring our souls into the world, or are they evoked by circumstance?

— George Moore

Aphorisms of Maimonides

(1135-1204)

Part II*

13. Special care should be taken to have regular movements of the bowels that carry off the impurities of the body. For this purpose young people should be given salty food, materials that have been soaked in olive oil, salt itself, or certain vegetable soups with olive oil and salt. Older people should take honey mixed with warm water early in the morning and four hours later should take their breakfast.

14. Another axiom of medicine is that so long as a man is able to be active and vigorous, does not eat until he is over-full, and does not suffer from constipation, he is not liable to disease.

15. Immoderate eating is a poison for men and the cause of many diseases which attack them. Most diseases come from either eating too much or partaking of unsuitable food. That was what Solomon meant with his proverb: "He who puts a guard over his mouth and his tongue protects himself from many evils," that is to say, whoever protects his mouth from the over-indulgence in food and his tongue from unsuitable speech protects himself from many evils.

16. Every week at least a man should take a warm bath. One should not bathe when hungry, nor after eating until the food is digested, and bathe the whole body in warm but not too hot water and the head in hot water. Afterwards the body should be washed in lukewarm and cool water until finally cold water is used. One should pour neither cold nor even lukewarm water on the head, nor bathe in cold water in the winter time, nor when the body is tired and in perspiration.

17. As soon as one leaves the bath one should cover oneself, and especially cover the head, so that no draught may strike it. After this one should rest for a while until the heat of the body passes off and then should go to table. Neither during the bath nor immediately after it should cold water be drunk, and if there is an unappeasable thirst a little wine and water or water and honey should be taken.

18. Venesection should not be practiced frequently, for it is only meant for serious illness. After passing his fiftieth year an individual should abstain from venesection. Venesection should not be practiced on the day when one takes a bath or goes on a journey or returns from it. On the day when it is practiced less than usual should be eaten and drunk, and the patient should give himself to rest, undertake no work nor bothersome occupation, and take no walk.

19. Whoever observes these rules of life faithfully I guarantee him a long life without disease. He shall reach a good old age, and when he comes to die will not need a physician. His body will remain always strong and healthy, unless of course he has been born with a weak nature, or has had an unfortunate bringing up, or should be attacked by epidemic disease or by famine.

20. Only the healthy should keep these rules. Whoever is ill or a sufferer from any injuries, or has lost his health through bad habits, for him there are special rules for each disease, only to be found in the medical books. Let it be remembered that every change in a life habit is the beginning of an ailment.

See Minnesota Med 50:320, 1967.

Benign and Malignant Gastric Ulcers

Diagnostic
Accuracy
X-ray
Examination
in
Differentiating*

JOHN BARTNESS, M.D.
Albert Lea, Minnesota

THE PREHISTOLOGICAL differentiation of benign and malignant gastric ulceration has long been a medical enigma. Up to the present time there is still no completely infallible method of differentiation. Brown et al.¹ concluded from their study of 106 cases of malignant gastric ulcer that no clinical symptom is specific in any way for carcinoma.

The purpose of this study was to determine the accuracy of the latest methods of roentgenological examination combined with meticulous scrutiny of the gastric mucosa by the examining roentgenologist.

Materials and Methods

One hundred fifty consecutive cases of gastric ulcer diagnosed by x-ray over a three-year period from mid-1963 to mid-1966 were reviewed. In all cases either x-ray or surgical follow-up studies were made. There were 88 male and 62 female patients. The youngest was 15 and the oldest, 89 years. The average age was 54.3 years. Because the study was concerned primarily with the accuracy of present methods of roentgenological diagnosis and directed rather rigidly at the morphological characteristics of the ulcer and surrounding mucosa, history, physical examination, laboratory studies, or any other factor which might influence the x-ray diagnosis, was not taken into consideration. Image intensification and cineradiography were used routinely on all patients. A nine-inch mirror and closed circuit television with magnification switch were used interchangeably. Anteroposterior, lateral, and posterolateral radiographs as well as spot films were made on every patient.

In each case the pliability of the gastric mucosa immediately adjacent to the ulcer crater, as well as the more distant mucosa,

*Presented at the Annual Meeting of the Southern Minnesota Medical Association, September 16, 1966, in Austin, Minnesota. Received annual award for the most outstanding paper presented at the time.

was noted and the morphological characteristics of the crater, of the edges of the crater, and of the surrounding mucosal pattern, were very carefully examined. Since almost all stomachs contain swallowed air, an automatic double air contrast study was easily obtained in the majority of patients by placing them in the supine position. This double air contrast effect is very clear when viewed directly with image intensification and indirectly with cineradiography, and was extremely helpful in increasing the clarity of the ulcer margins and the detail of the adjacent mucosa.

Nature of the Ulcers

Most of the ulcers were found in the lesser curvature of the antrum. See Table 1 for details.

TABLE 1

Lesser curvature of the pars media	45
Greater curvature of the pars media	4
Lesser curvature of the antrum	86
Greater curvature of the antrum	8
Prepyloric	6
Lesser curvature of the cardia	1

Size of Ulcers

The ulcers varied in size from 1.5 mm. to 5 cm. The size of the ulcer also had no bearing on the radiological diagnosis.

Associated Duodenal Ulcer

Thirty patients had accompanying duodenal ulcers. However, this did not influence the study in any respect. Lampert et al.² found in their study of malignant gastric ulcers that 21.9 percent had accompanying duodenal ulcers.

A statement as to whether the ulcer was benign or malignant from an x-ray standpoint was included in the x-ray report of each patient. If the ulcer was thought to be radiologically benign, repeat x-ray studies were done following two to ten weeks of medical management. Gastric ulcers were considered proven benign if follow-up x-ray studies revealed that the crater and any edema of the adjacent mucosa had completely disappeared. Meireles et al.³ have concluded from a study of 250 gastric ulcers,

that a gastric ulcer which disappears completely with obliteration of the crater and no evidence of stiffening of the adjacent gastric wall may be safely accepted as benign.

Results

Of 143 gastric ulcers labeled benign on x-ray examination, all 143 were found to be benign by follow-up x-rays or surgery.

Case One

In one patient, a 59-year-old white female, a 2.5 cm. ulcer crater was demonstrated on the greater curvature of the antrum. A second ulcer, slightly smaller, was found on the lesser curvature of the pars media of the stomach. Both ulcers were called radiologically benign. The examination was repeated six weeks after medical management. Both ulcers had increased in size but were again labeled benign by x-ray examination. A third examination was done three months after continued therapy. The ulcers remained the same in size but were again called radiologically benign. A gastric resection was performed and both ulcers were found to be histologically benign.

Case Two

A 50-year-old female was found to have an ulcer crater 3.5 cm. in diameter located on the greater curvature of the antrum. The ulcer revealed no radiographic characteristics of malignancy. Three subsequent examinations at six-week intervals failed to show any change after medical management and the ulcer was still diagnosed as benign by x-ray. Surgical exploration and gastrectomy were performed and the ulcer declared histologically benign.

The Malignant Ulcers

Four gastric ulcers which were called malignant on x-ray examination were found to be histologically malignant following surgical removal. Stiffness of the mucosa adjacent to the ulcer crater and intraluminal hypertrophy of the margins of the crater (Carman's meniscus sign) with minimal mucosal edema were demonstrated in two of the cases. A third case revealed a broad, shallow ulcer crater with stiffness of the mucosa around it and a small degree of prominence of the edges of the crater. The ulcer of the fourth patient was 1 cm. in diameter and located on the greater curvature of the antrum. No decision was made on the first examination; however, on repeat examination a vague lack of pliability of the mucosa around the ulcer was noted. In addition, edema with spasticity was demonstrated

throughout the antrum probably due to concomitant antral gastritis.

The Suspiciously Malignant Ulcers

The three remaining cases in the study were called malignant from a radiological standpoint but were proven to be benign. One was a 50-year-old male with an ulcer crater 3 cm. in diameter on the greater curvature of the pars media. The crater was shallow, showed minimal elevation of the ulcer margins, and stiffening of the crater itself as well as the surrounding mucosa. Surgical exploration revealed a benign gastric ulcer with chronic perforation into the body of the pancreas. Histological specimens revealed considerable localized chronic inflammatory reaction. A second case showed definite intraluminal building-up of the margins of the crater. Subsequent surgery revealed a benign ulcer. Although building-up or hypertrophy of the ulcer margins may be extremely helpful and arouses the suspicion of malignancy, it is not a pathognomonic sign in differentiating benign and malignant gastric ulcers. Nevertheless, it is felt that such cases should be surgically explored. The last patient, a 65-year-old female, had a greater curvature antral ulcer with mucosal edema and elevation of the ulcer margins. Although there was no demonstrable mu-

cosal stiffening, surgical exploration was advised because of the intraluminal hypertrophy of the ulcer margins. Surgery was deferred because of a cardiac condition and re-examination by x-ray four weeks following a semi-ulcer diet revealed that the ulcer had completely disappeared.

Conclusions

The purpose of this study was to determine the accuracy of the latest methods of roentgenological diagnosis in differentiating benign and malignant gastric ulcers. One hundred and fifty consecutive cases of gastric ulcer diagnosed by x-ray over a three-year period were included in the study. One hundred and forty-three gastric ulcers were called benign on x-ray examination and were proven to be benign by follow-up x-rays or surgery. Four gastric ulcers were labeled malignant on x-ray examination and all four were found to be malignant following surgery. Three gastric ulcers were diagnosed as malignant by x-ray and were found to be benign by follow-up x-rays or surgery.

The refinement of current methods of roentgenological examination and the adaptation of the radiologist to these methods are believed to be significant factors in lessening the percentage of error in differentiating benign and malignant gastric ulcers.

References

1. Brown, Paul M., Cain, James C., and Dockerty, Malcolm B.: Clinically "Benign" Gastric Ulcerations Found to be Malignant at Operation. *Surg Gynec Obstet* 112:82, 1961.
2. Lampert, Elmer Graham, Waugh, John M., Dockerty, Malcolm B.: The Incidence of Malignancy in Gastric Ulcers Believed Preoperatively to be Benign. *Surg Gynec Obstet* 91:673, 1950.
3. Meireles, Jos'e De Souza, Jr., Montenegro, Mario Rubens, Zaterka, Agostinho Bettarello, and Pontes, Jose' Fernandes.: A Comparison of Roentgenologic and Histologic Data, *Amer J Dig Dis* 7:661, July 1962.

Ten Commandments for Doctors

1. Don't keep your patient waiting.
2. Discuss your fee frankly with him.
3. Explain disease and treatment to him.
4. Let the patient talk.
5. Don't ask the impossible of him.
6. Don't divide your attention.
7. Know his family.
8. Tell him the truth.
9. Relieve his anxiety.
10. Try to like him.

— Martin Gumpert, M.D.

You and Your Doctor, Bobbs-Merrill, 1952

One of Laennec's Cases

In 1816 I was consulted by a young woman who presented general symptoms that pointed to the existence of some disease of the heart, and in whom, by reason of her embonpoint,* simple palpation and percussion could scarcely be expected to furnish satisfactory information in regard to the nature of the disorder. The age and sex of the patient not permitting me to make such an examination as I have just mentioned I was compelled to adopt some other measure; and I then recalled to mind the acoustic phenomenon with which everybody is familiar, to-wit: if the ear be applied to one end of a wooden beam it will perceive with perfect distinctness the sound made by the scratching of a pin's point on the opposite end of the beam. From this circumstance I inferred that in the present case I might advantageously utilize the principle underlying this phenomenon. Accordingly I rolled up into a cylinder-shaped, stiff-walled tube several sheets of writing-paper, and, resting one end of the clinder on the skin of the precordial region, I applied my ear to the other end of the tube. I found to my surprise and pleasure that I was now able to hear the pulsations of the heart much more distinctly than I had ever before heard them when I applied my ear directly to the chest-wall.

— Laennec, Rene (1781-1826)

*See Test Your Word Score Page 521.

Unamuno, the Agonist

"I Want to Live"

"I do not want to die — no; I neither want to die nor do I want to want to die; I want to live for ever and ever and ever. I want this "I" to live — this poor "I" that I am and that I feel myself to be here and now, and therefore the problem of the duration of my soul, of my own soul, tortures me."

These anguished words came from the naked soul of the existentialist Spanish philosopher, Miguel de Unamuno, who was obsessed by the irreducible contradiction between faith and reason: the heart's desire for immortality and the mind's awareness that man must die.

Annihilation being inconceivable and immortality undemonstrable, Unamuno had to admit the existence of the dichotomy; but in his agonizing doubt and despair he advocated that man not meekly resign himself to but valiantly fight against the paradox he himself had produced but could never resolve.

This heroic but vain struggle is the theme of Unamuno's two books, "Tragic Sense of Life" and "The Agony of Christianity," both placed on the Papal Index, although, ironically, their author was a Catholic.

On Quaffing

Nothing can hold liquor as well as a bottle. So leave it in the bottle.

— Rail and Tie



Editorials

Milk Sickness*

MILK SICKNESS was a disease of considerable importance to public health in the pioneer settlements of Tennessee, Ohio, Indiana, Illinois, and Missouri. This disease was described as early as 1776 in North Carolina, but for more than 100 years the cause remained unknown. Today, although this disease is becoming a medical curiosity, it is interesting to speculate on the reasons why the cause of milk sickness, which ravaged so many pioneer families and their livestock, remained obscure for such a long time.

We now know that milk sickness in man and trembles in animals are caused by tremetol, a complex alcohol found in two perennial herbs: white snake root and rayless goldenrod. White snake root is seen in woods of all types and along streams in wooded pastures in the middle west. Rayless goldenrod is found on the dry plains, grasslands, and open woodlands of the southwestern part of the United States.

As pioneer families established farms west of the Allegheny mountains, they first cleared land for crops and gardens, leaving their livestock to browse the adjacent wood-

land. Since wooded areas do not have the grazing potential of cleared areas, livestock were often vulnerable during the summer months to the effects of browsing white snake root plants. Cows giving milk were especially vulnerable because of the demand for additional nutrients necessary in milk production. However, the lactating cow was often able to survive by excreting tremetol into the milk. Thus, as man drank the milk or ate milk products, he became an unsuspecting victim of milk sickness.

These pioneers were seeing a new disease not observed on the eastern seaboard or reported in European medical literature. Not having the knowledge of present-day botanists, these newcomers did not know that only one of more than 40 species of white snake root (*Eupatorium urticaefolium*) was poisonous. If we realize that at the time there were few veterinarians and physicians, that the scientific method was unknown, and that medical communication among the frontier doctors was almost lacking, then we can understand the painfully slow progress on the etiology of milk sickness.

Paul E. Zollman, D.V.M.
Rochester, Minnesota

*See page 469.

We Wonder!

Why did Nature create man? Was it to show that she is big enough to make mistakes; or was it pure ignorance? — Holbrook Jackson

In peptic ulcer... antacid therapy with a new benefit



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Stuart

Cardiopulmonary Resuscitation*

THE MODERN techniques of cardiopulmonary resuscitation are sufficiently easily understood and carried out that they may be successfully employed by teams or individuals who may not be physicians. The article, "Restoration of Cerebral Physiology: An Unusual Case of Cardiac Resuscitation" by Dr. Leroy Ekstrand serves to illustrate the kind of team effort Ekstrand worked to produce. This kind of effort on his part will certainly be a monument to his memory in his community.

There are two stages to cardiopulmonary resuscitation in terms of time. The first is the institution of closed-chest cardiac massage or mouth-to-mouth resuscitation, or both, as soon as a cardiac or a pulmonary emergency occurs. Brain damage can be expected to begin four to six minutes after effective circulation stops. If resuscitation is to have a chance of succeeding, it must be

instituted by people on the scene, without waiting for the arrival of a physician. The second stage consists of electric defibrillation, the use of pressor agents, agents to combat acidosis, cardiac pacemakers, and the many highly technical procedures that require a physician, a hospital, and, hopefully, an intensive care facility. The patient can benefit by the second-stage procedures only if trained persons are ready to treat him in the brief six-minute time limit of the first stage.

Each community can follow the example of Dr. Ekstrand and the firemen he trained. Training exercises using a manikin, films, and demonstrating devices will help to produce teams of competent people. The physicians of the community are in a unique position to act as teachers in this field and extend the possibility of saving lives.

John A. Callahan, M.D.
Rochester, Minnesota

*See page 487.

The Diagnosis of Gastric Ulcer*

IN THE MANAGEMENT of gastric lesions, surgery is often employed as a diagnostic method as well as a therapeutic one. If other diagnostic methods were more exact, wiser therapeutic choices could often be made between non-operative medical management and a preplanned surgical approach.

We have generally overburdened the radiologist by the weight of responsibility placed on his techniques and ability, whose accuracy only timely repeated examination or surgery — or autopsy, can verify. This is still relatively true despite the undoubted real improvement in x-ray diagnosis consequent to the use of cineradiography. The results of these techniques used prospectively by well-trained persons are reported elsewhere in this issue and represent the impressive ultimate and extraordinary results of such efforts. They are extraordinary in that techniques employed do not yet represent the usual diagnostic facilities available to

the majority of patients. They are ultimate in that this is a degree of excellence for all to seek. One means of approaching this diagnostic accuracy generally is to make modern radiographic techniques and abilities more generally available, and this is happening. Another is to improve other complementary and validating diagnostic methods. This too, is happening.

Recent technical developments in flexible fiberoptic lighting and viewing systems and in photographic equipment have moved direct intragastric visualization into first line position, importantly complementing x-ray techniques. Our own reasons for this conclusion are based on the experience gained in over 1,000 examinations using primarily the GTF Olympus Fiberoptic Gastroscope Camera.** They are supported by the increasing utilization of these same techniques by other interested persons in this medical community and by the reported experience of others using the same¹ and other fiberoptic

*See page 505.

**Olympus Corporation of America, Long Island City, New York.

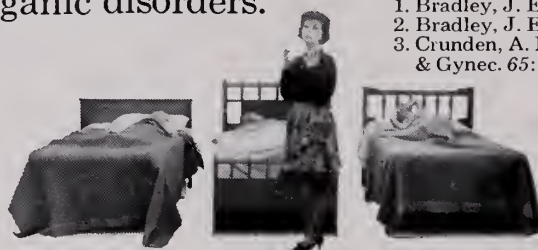
Continued



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1. Bradley, J. E., *et al.*: J. Pediat. 38:41 (Jan.) 1951.
2. Bradley, J. E.: Mod. Med. 20:71 (Oct. 15) 1952.
3. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. 65:311 (Feb.) 1953.



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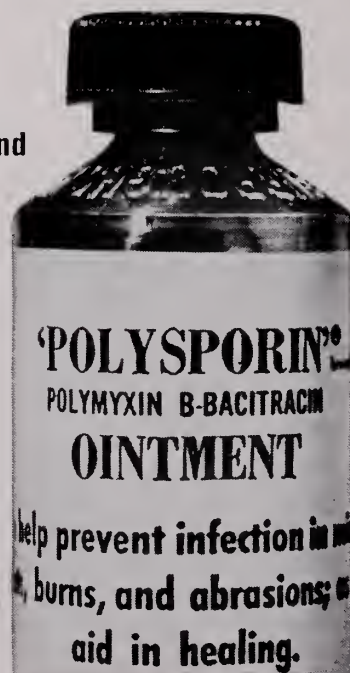
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equipment elsewhere.^{2,3} As compared with earlier equipment, procedures using flexible fiberoptic systems are not traumatic or morbid, thus becoming applicable to more patients. Blind areas are consistently reduced. Easily obtained, good quality color film records allow serial comparison and follow-up of a given lesion, removing the variables of imperfect recall by one endoscopist. Also, film comparison with other similar lesions has tremendous teaching value, as does the direct endoscopic "panavision" view of the stomach.

Most importantly, modern gastroscopy is an accurate diagnostic technique. Of 170 proven gastric ulcers evaluated during the past three years at the Minneapolis Veterans Hospital by both x-ray and endoscopic techniques, fiberoptic gastroscopy and photography has been employed in the majority. Only two lesions were not visualized on initial examination with this equipment. All of the 10 malignant ulcers in the series were correctly diagnosed endoscopically. Of the 158 benign ulcers seen, nine were initially called probably malignant gastroscopically, but were proven benign on histologic examination of surgical specimens. Four of these were thought to be malignant by the surgeon examining the lesion grossly.

Evaluation of any diagnostic technique must consider not only the accuracy with which the specific pathologic process is identified, but also the accuracy with which all existing lesions in patients studied are discovered. The latter is difficult in evaluating clinical techniques since not all studied patients come to direct surgical or autopsy comparison. Evaluation of our experience is further hampered by the fact that examinations on very active and busy teaching endoscopy and x-ray services are done by supervised resident trainees in gastroenterology or radiology. The latter do most routine work with conventional x-ray techniques, employing occasional cineradiography. Therefore, our experience cannot be closely compared with that of fully-trained examiners. Nevertheless, it is noteworthy that of the 170 gastric ulcers proven by any means, we missed two benign ulcers endos-

copically, while 58 benign ulcers and four malignant ulcers would have been missed on initial examination had not gastroscopy been performed.

Finally, modern day gastroscopy can so completely examine the stomach, with such good optical resolution that diffuse mucosal abnormalities such as mucosal atrophy or hypertrophy, and notably acute antritis can now be identified and studied further. Gastric pathology has long suffered for the lack of such gross correlates. We are also prospectively studying the means by which fiberoptic gastroscopy and cineradiography may complement each other in the important discovery of sources of acute upper gastrointestinal hemorrhage.

All gastric ulcers should be initially regarded as suspicious for malignancy until all possible characteristics are defined. However, not all gastric ulcers need any longer be immediately removed surgically. If the lesion appears quite definitely benign radiologically and/or endoscopically, it should be determined that on full ulcer regimen progressive healing occurs on serial examination. Follow-up study at least once within three months of apparent healing is advisable. Non-healing in three weeks or incomplete healing in six weeks should make early operation a very serious consideration. "Apparent" healing of malignant ulcers has been noted, though infrequently, and if carefully examined, most of these lesions will have other characteristics which place them in the next group rather early.

This next group includes those lesions whose benignancy is variably questionable on initial study. These should be promptly and thoroughly studied by cineradiography and gastroscopy when available and, depending on the assessment of malignant probability, either operated at once or followed for one or two weeks and re-studied. The latter approach is justified at times because edema around a benign, usually antral, ulcer can be indistinguishable from infiltration with stiffness and loss of peristalsis. On re-examination after even 7-10 days of ulcer management, the appearance may be more

Continued

There are 36,700* undetected diabetics in Minnesota

Most of these are probably among patients over 40; the overweight; relatives of diabetics, and mothers of large babies. By the time polyphagia, polyuria, polydipsia, pruritus or other overt symptoms of diabetes appear, damage may have been done that could have been minimized. DEXTROSTIX® gives you a reliable blood-glucose estimate in 60 seconds.

Why Wait?



*Based on Statistical Report, U.S. Dept. Commerce, ed. 86, and Fisher, G. F., and Vavra, H. M.: Pub. Health Rep. 80:961 (Nov.) 1965.

Note: DEXTROSTIX is not meant to replace the more precise analytical laboratory procedures such as needed in glucose tolerance testing.

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Ames

evidently benign and can then be cautiously followed for a short period.

As a general attitude, while diagnostic methods are becoming more accurate and available, we must continue to err on the side of "over-calling" malignancy and to follow gastric ulcers closely, since not even the gross appearance always distinguishes be-

tween benign and malignant ulcer. This is particularly important since early operative management of the malignant ulcer apparently offers a substantially better prognosis than that of all gastric malignancies.

Jack A. Vennes, M.D.
Gastroenterology Section
Minneapolis Veterans Hospital

References may be obtained from the author.

Amebic Liver Abscess

THE ARTICLE by Doctors Farley and Linner in this issue of MINNESOTA MEDICINE* makes it amply clear that no longer can we regard tropical diseases and parasitic infestations as interesting but vague entities of our medical school parasitology course to be forgotten as we go out to practice in the temperate climate of Minnesota. The airplane and the "guided tour" have brought vacations to Mexico, Central America, South America, and even Africa and the Orient within the financial and time budgets of many Americans. By the thousands, Americans (including Minnesotans) are flocking to these areas, endemic for protozoan and parasitic diseases. Those becoming infested, may manifest no symptoms until long after their return home. The unwary Minnesota physician confronted with a bizarre symptomatology may be led completely astray unless the travel history is elicited, and it leads him to search for tropical diseases by the special diagnostic procedures available.

The finding of three cases of amebic hepatic abscess at one community hospital in Minneapolis in a three-year period attests to the fact that this entity is not as rare as many physicians in this area would believe.

The diagnosis of amebiasis is not always easily made. If the stool and proctoscopic examinations are negative, one may have to proceed with treatment on clinical grounds alone. Recently a hemagglutination test has been devised which gives strong supportive evidence when the above examinations are negative. Unfortunately, the test is not generally available and is run only by the Com-

municable Disease Center in Atlanta, Georgia, on blood specimens submitted through the various State Health Departments. In a critically-ill patient, treatment may have to proceed before the diagnosis is confirmed.

Patient 2 in the article by Farley and Linner had a positive hemagglutination test which was not reported until after treatment was completed.

The recent development of the technique of liver scanning with radioactive gold or radioactive rose bengal has added a useful tool for the diagnosis of amebic liver abscesses. Although the scan does not give a definite diagnosis, it does locate a space-occupying lesion within the liver and directs attention to the advisability of surgical drainage; furthermore, it helps guide the probing needle of the surgeon. Surgery on a case of amebic hepatitis without abscess would be inadvisable; but the scan here would be expected to be negative.

Treatment of suspected amebiasis either alone or with hepatic abscess should not be delayed in the seriously-ill patient even if proof of the diagnosis is lacking. On the other hand it should be recognized that anti-amebic therapy, especially emetine, may be toxic. Heart damage may ensue from emetine and may be permanent. Farley and Linner's Patient 2 did develop considerable electrocardiogram change which fortunately was transient. A peroneal nerve palsy did remain as a permanent residual in that case, presumably due to the emetine, but perhaps just a result of his debilitated state.

Markle Karlen, M.D.
Minneapolis, Minnesota

*See page 477.



Photo professionally posed

Mike expects a penicillin injection. He's about to be pleasantly surprised.

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Information Systems Technology as an Aid to Medicine

PHYSICIANS, FOR the most part, have not experienced the professional stresses that the advent of automation has thrust upon those working in industry. It is essential for the medical profession to prepare itself for radical changes which it soon must face. These changes are exemplified by Dr. Morris Collen's* pioneer work in California in the utilization of data-processing techniques for providing periodic health check-ups to large numbers of people.

A physician functions in two ways: as data collector and processor and as decision-maker. He collects, abstracts, and records data regarding each patient and then compares this data with prior medical experience to make diagnostic and therapeutic decisions. To provide up-to-date health care for his patients the physician of today faces two enormous problems: the problem of ef-

ficiently collecting and processing data on the individual patient among his rapidly increasing number of patients, and the almost hopeless problem of retrieving rapidly for medical decision-making pertinent data from a medical literature which, it is estimated, is doubling in quantity every 10 years. The new technology of electronic data processing and its extension into control of automated machines promises enormous aid toward the solution of these problems. However, it may be that solutions can be achieved only by accepting radical changes from the traditional methods of thinking and acting in current medical practice. Education and preparation for extensive change are essential, if we are not, collectively as a profession as well as individually as members of a changing society, to find ourselves disorganized and unable to cope rationally with a new professional environment.

John G. Mayne, M.D.
Rochester, Minnesota

*Collen, Morris F: Computer Medicine. Minnesota Med 49: 1705, 1966.

Boustrophedonic Scanning of the Lung

BOUSTROPHEDONIC* SCANNING of the lung following the injection of radionuclide-labeled macroaggregated albumin has proved to be a powerful new tool in the assessment of pulmonary function.

From the original brilliant idea of Bénacerraf and associates¹ in France, colloidal material was developed as a lung-scanning agent in this country, largely by Taplin and associates.² Numerous other reports have subsequently appeared in the literature.

This method was developed originally for the detection of pulmonary emboli, but although it performs this task quite well, this has proved to be one of its less important uses; it seems to be a much more widely applicable tool.

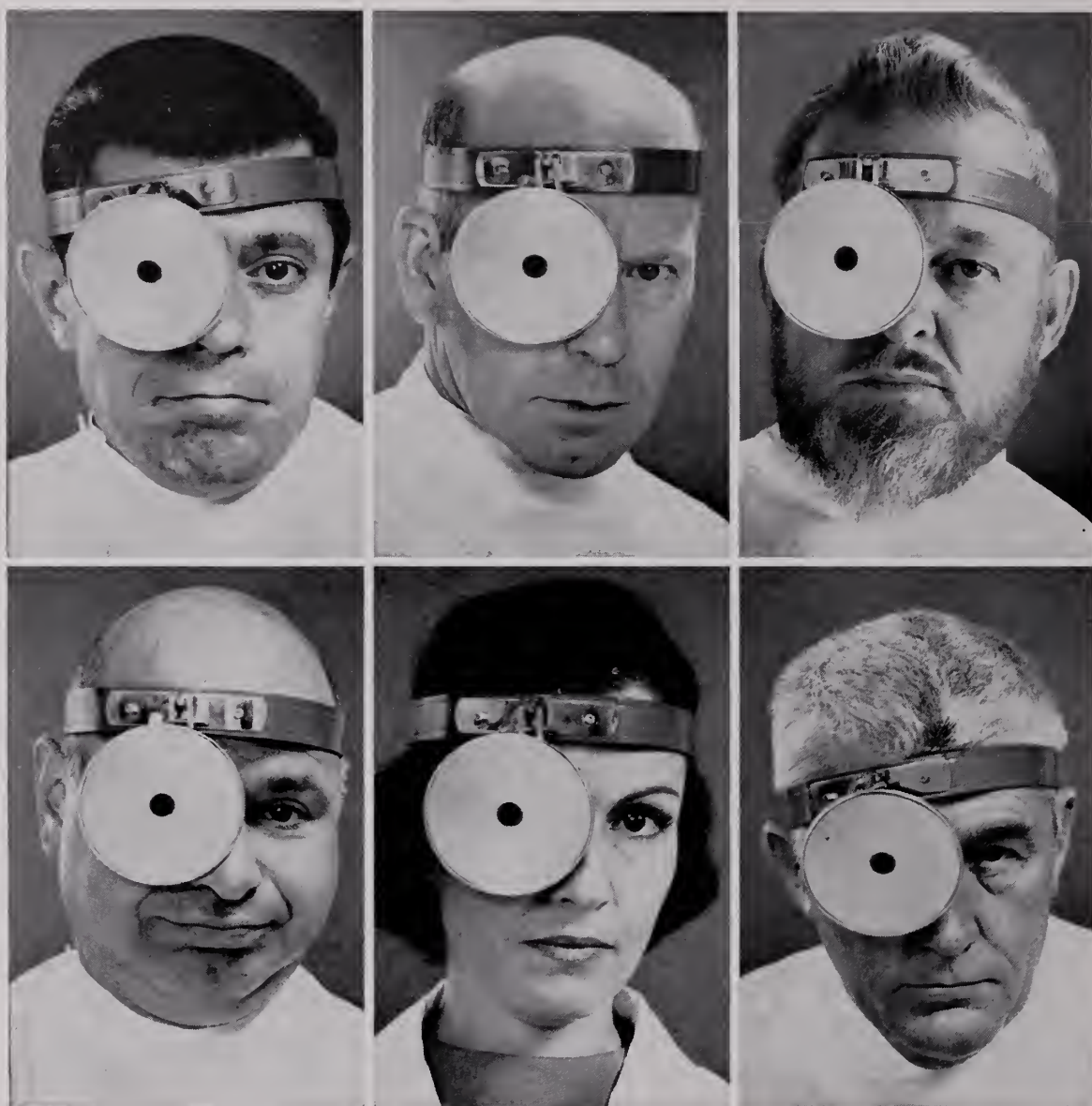
When injected into the peripheral vein, the macroaggregated albumin seems to follow the path of the venous blood from that vein and to lodge for a period of an hour or so in the first capillary bed it encounters,

normally in the lung. Since usually it is cleared almost completely by the lung, it affords an excellent index of pulmonary blood flow. Indeed, early evidence now indicates that when digital computing devices are applied to scan data, quantitative information may be obtained.³ In the presence of a right-to-left shunt, total count rates over the lungs apparently decrease by approximately the degree of the shunt.

The lung scan has been of great value in indicating the distribution of blood within the lung, including the striking effects of gravity on pulmonary flow. Scans from patients injected in a feet-down position show that the blood flow is predominantly basal and that almost no flow from the right ventricle reaches the apex, which supports the old theory of the apical distribution of pulmonary tuberculosis. After injection in a feet-up position, the flow is predominantly apical. This varying distribution is most striking in subjects who have large lungs, in

*See Test Your Word Score Page 521.

Continued



"All Otolaryngologists are Alike"

Just look at them and you can see how much they have in common. Besides, they all go through pretty much the same training, and pass the same kinds of tests, and measure up to the same sort of standards. Therefore, all otolaryngologists are alike. Right?

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You might also say that all otolaryngologists aren't alike, either.



which dependent filling is a constant finding.

In patients with increased left mean atrial pressure, pulmonary flow is predominantly apical, and this finding supports the old theory of Virchow which explains why patients with mitral stenosis have a low incidence of tuberculosis. Computerized scans may afford a good index of left mean atrial pressure.

One of the most striking aspects of pulmonary scans is that they are so often positive and correlate with pathologic processes in the face of negative roentgenograms of the chest.⁴

*Mayo Clinic and Mayo Foundation.

References may be obtained from the author.

Chest roentgenograms give basically architectural information; lung scans provide basically functional information specifically relating to pulmonary blood flow. Other facets of this diagnostic technique currently under consideration are inhalation scans and scans following injection of gamma ray-emitting gases (xenon-133).

The pulmonary scan seems to be extremely safe, is easy to perform from the patient's standpoint, and provides a great deal of information. It is likely to prove a diagnostic tool that will last.

W. Newlon Tauxe, M.D.*
Rochester, Minnesota

Stapedectomy

RENEWAL OF A forgotten procedure with the advent of the surgical microscope and associated tools and techniques has placed the availability of near normal hearing to many who suffer from a particular type of conductive hearing loss; i.e., that due to fixation of the stapes. Despite the fact that little is known of the etiology of the diseases that produce fixation of the stapes, correction in the majority of patients achieves results that can hardly be matched by many surgical procedures.

It requires the patient to lie quietly for one to two hours with the head turned to the side. A local anesthetic is injected into the ear canal. The operative field is confined to the ear canal and middle ear. Exposure is obtained by elevating a flap of canal skin and the attached ear drum forward. The stapes is either removed or remodeled and the ossicular chain is reconstructed with a variety of techniques, most of which give good hearing results.

Complications occur rarely. Vertigo is common in the immediate postoperative period but usually subsides in a few days. The most serious complication is complete loss of hearing in the operated ear. This fortunately occurs rarely. The various complications as enumerated by Barnett Eades*

in the November issue of MINNESOTA MEDICINE should be foremost in the mind of the surgeon in evaluating candidates for surgery but should not deter the family physician in recommending an otological examination for the possibility of surgical correction of hearing loss.

Not all patients with hearing loss will benefit from stapedectomy. Those patients who have a gradual progressive hearing loss that begins between adolescence and early adult life may have otosclerosis. It is familial and occurs more frequently in women than in men. These patients hear better in noise than in quiet surroundings because of the increase in volume of the speaker's voice. Air and bone conduction audiometry and tuning fork tests confirm the diagnosis.

Those patients who have fixation of the stapes at birth from congenital causes may not be diagnosed as hard-of-hearing patients until they are several years old, and the time of onset and therefore the type of pathology present may be obscure. Whatever the cause of the stapes fixation, whether congenital, otosclerotic, or associated with other bone defects such as osteogenesis imperfecta, the treatment is stapedectomy, fenestration of the oval window, and insertion of a prosthesis. The optimum time of surgery, however, may vary in the different

*See Complications of Stapedectomy, MINNESOTA MED 49:1743, 1966.

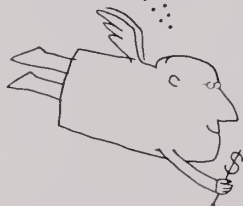
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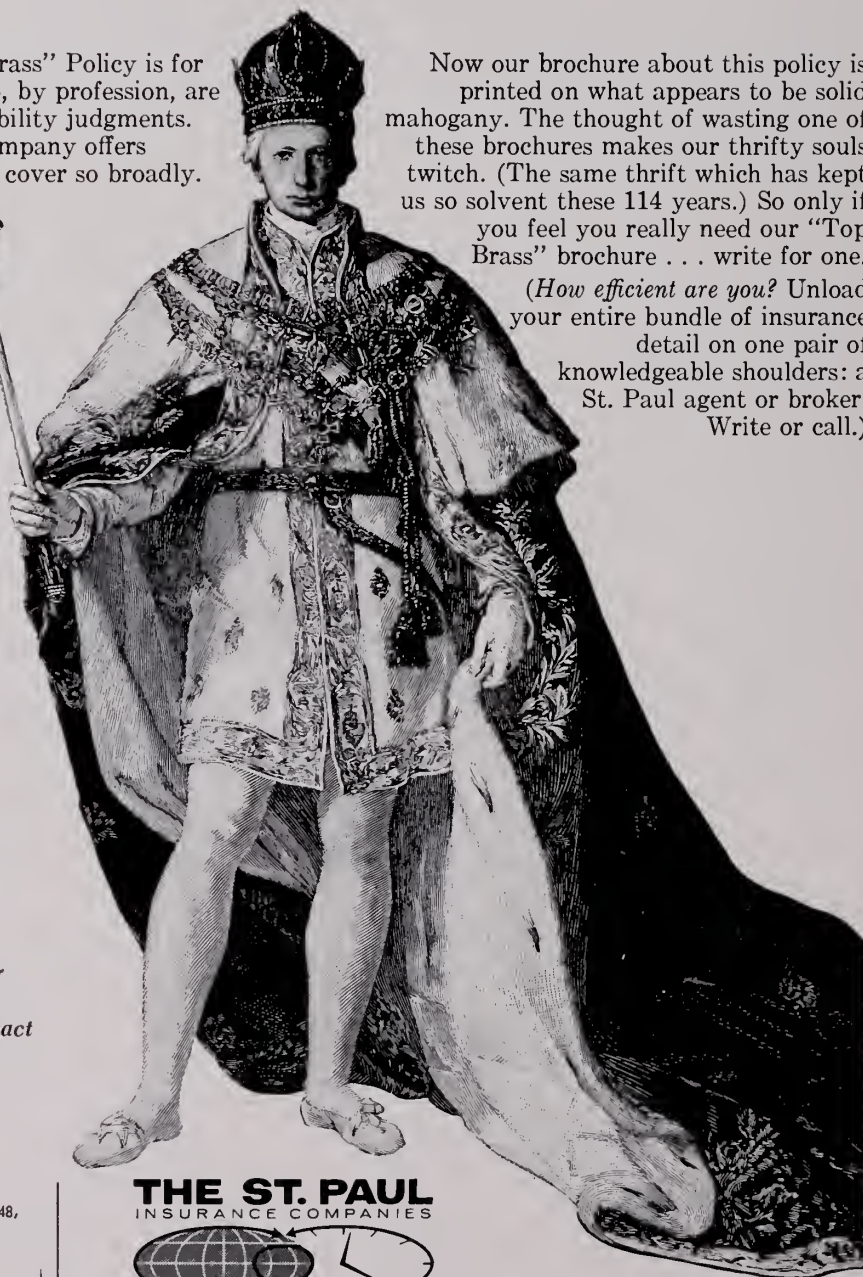
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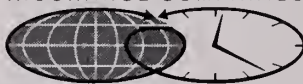
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types of pathology. Those patients who cannot understand speech even with volume or who are confused by several people speaking will probably not benefit from stapedectomy because they probably have a sensori-neural problem. This is ascertained by testing the patient's ability to understand speech.

Attempts at restoration of hearing were successful by mobilization of the stapes prior to 1900 but were discontinued. One can speculate that lack of magnification, lack of proper illumination, and unavailability of antibiotics produced complications that outweighed the advantages of surgery. Continued interest in restoration of hearing by surgical means produced the fenestration operation which was refined by Lempert. This was a meticulous and tedious operation that improved hearing but could not restore it to the normal level. However, Rosen rediscovered stapes mobilization inadvertently, and the hearing gain that ensued was so much better than the results from fenestra-

tion, and the procedure itself was so much simpler, that this became the acceptable procedure for restoration of hearing in cases of clinical otosclerosis. It became apparent, however, that many of these mobilized stapes could refix and the hearing loss could again return. Shea proved that the stapes could be removed completely and the ossicular chain reconstituted with artificial material. This produced a more permanent hearing gain. Variations of this technique with either partial or total stapedectomy with insertion of various types of prostheses is the standard operation today for clinical otosclerosis.

Microsurgical techniques are truly modern advances in medicine. They have been refined to the point where further advances in this direction are not likely. Further investigative efforts directed toward etiology of otosclerosis will undoubtedly prevent not only the conductive component but the cochlear (sensori-neural) component as well.

John S. Huff, M.D.
Minneapolis, Minnesota

Test Your Word Score

Trembles — *a disease of cattle and sheep, characterized by weakness and possible stumbling and falling (page 471).*

Ratafia — *any liqueur flavored with fruit or fruit kernels, especially bitter almond (page 481).*

Makrobiotik — *from macrobiotics: the art or science of prolonging life (page 482).*

Analog — *That which is similar to another thing (page 483).*

Atresia — *pathologic closure of a normal opening (page 491).*

Embonpoint — *obesity (page 508).*

Boustrophedonic — *resembling an ancient mode of writing alternate lines in opposite directions: e.g., line 1 to the right and line 2 to the left (page 517).*

Phenotype — *a type determined by common visible characters as distinguished from hereditary characters (page 541).*

Rumpel-Leede test — *a test for the presence of minute subcutaneous hemorrhages forming under a not-too-tight rubber band applied to the upper arm (page 545).*

Isosmotic — *having equally effective concentrations of actively soluble components (page 574).*

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The Editor's Soliloquy

Don't Rest Yourself to Death

There is no such thing as overwork. A man may die with his boots on: he may die while at work from systemic disease or an accident — but not from work per se. Work of any kind, whether physical or mental, white-collar or blue-collar, can cause fatigue or even exhaustion; but it does not cause death. For with fatigue comes sleep and with sleep comes revitalization, preparing the individual for another day's work in man's diurnal pattern of alternating labor and rest.

Some individuals almost boast of working themselves nearly to death; they comprise a brotherhood of the chronically tired. Such a poor mortal is always insisting that he needs more rest. He requires a nap after breakfast, a mid-morning coffee break, a noon siesta, and an afternoon cigaret break. After work and before dinner he feels the urge for a brief snooze or a relaxing cocktail. He has had such a hard day! Ergo, he needs more rest; and the more he gets, the more he wants. Deciding finally that something must be wrong, he consults a doctor who, not having analyzed his patient's faulty rest habits, pronounces him sound. The very idea! So the vicious spiral continues.

Experimental studies have conclusively shown that in complete rest the body readily goes into a negative nitrogen balance, losing more nitrogen than it consumes, and that as the loss continues atrophy develops — despite a possible gain in weight. Physicians have long since discovered the tremendous healing value of early ambulation in the treatment of most diseases; and it has been repeatedly demonstrated that physical activity is one of the best physiotherapeutic agents available.

So let's liberate ourselves from that pernicious obsession that we are working ourselves to death and can't get rested up. Let's energize ourselves with constructive activities and attitudes so that at the end of the day healthy fatigue will induce natural and re-energizing sleep.

Let's repolarize our negative into positive physiologic and emotional values before we die of ennui and inanition by resting ourselves to death.

Carl O. Rice, M.D.

Vigorous writing is concise; A sentence should contain no unnecessary parts, a paragraph no unnecessary sentences. For the same reason that a drawing should have no unnecessary lines and a machine no unnecessary parts. This requires not that the writer make his sentences short, or that he avoid all detail and treat his subjects only in outline, but that every word tell.

William Strunk Jr., *Elements of Style*

Old Doc Dess Says: At the beginning — 40 years of productive life seem so long — at the end so short. — C. O. R.

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1. Schleif, R.H.: J.A.P.H.A., 46:179,1957 *U.S. Pat. No. 3,062,714
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Our Senior Educators



James R. Dawson, Jr., M.D.

WHILE THE OVERALL summation of the prolonged, complex and very substantial contributions of an academician is a difficult achievement for his own generation, the manner in which these contributions are made is readily apparent during his lifetime. There are few men who have moved through their tenure as departmental chairmen at the University of Minnesota Medical School with the modesty and thoughtfulness of Dr. James Robertson Dawson, Jr. In an era of increasing size and complexity of the Medical School and its component parts, Dr. Dawson has made a determined effort to maintain the integrity of the individual and to produce a harmonious department in which the maximum potential of his residents and staff would be manifested. To this purpose a great portion of his energy has been spent in encouraging and facilitating the academic pursuits of both his junior and his senior colleagues, often at a considerable sacrifice to his own personal endeavors.

The philosophical background which served to distinguish Dr. Dawson was instilled in him almost from the time of his birth in Birmingham, Alabama, on January 19, 1908. He was born into a family which had a proud medical lineage extending back for three generations. From

Continued

this heritage was bred a great security in the role of physician and likewise the sense of carrying forward an established tradition. His ancestral background also provided him with an extraordinary sense of ease, graciousness and good breeding which he retained in spite of his transplantation to the comparatively arctic northwest.

Dr. Dawson spent many years of his academic life at Vanderbilt University, receiving a Bachelor of Arts degree in 1928 and a Doctor of Medicine degree in 1931. He then became an Instructor in the Department of Pathology at Vanderbilt University Medical School, where he remained until 1934. A figure who stimulated him greatly was Dr. Ernest William Goodpasture, a pathologist of extraordinary ability, with whom Dr. Dawson had a prolonged and very close relationship. During this early portion of his medical career Dr. Dawson devoted much of his research effort to virology and particularly to viruses affecting the central nervous system. In 1934 he left Vanderbilt to become an Assistant in Pathology and Bacteriology at the Rockefeller Institute for Medical Research, where he continued his work in virology and worked very intensively with the rabies virus. Following a year at the Rockefeller Institute, he became an Instructor of Bacteriology and Immunology at the Cornell University School of Medicine, where he stayed until 1938, at which time he returned to Vanderbilt University School of Medicine as an Associate Professor of Pathology and subsequently became a full Professor in this department.

In 1949 Dr. Dawson came to the University of Minnesota School of Medicine as Professor and Head of the Department of Pathology. This represented both a great honor and a great challenge, since he was assuming the chair of Dr. E. T. Bell, one of the most outstanding medical figures in the history of the Medical School as well as in the field of pathology. Under Dr. Dawson's chairmanship the traditions of an excellent department were maintained and innovations introduced without disruptive effects. A feature which was to be constantly present during his tenure was immediately manifested, namely the effort to integrate the department in such a manner as to provide an opportunity for each member to devote the most time possible to those areas in which he showed the greatest interest and productivity. Thus from the beginning there was a department which worked harmoniously and with a feeling of maximum support from its department head.

Dr. Dawson has a commitment to the concept that the chairman of a department should devote himself to the academic advancement of individuals at all levels at which the department functions. Thus he has presented the majority of the lectures to the medical students; and with the residents he has devoted a great deal of time to reviewing their autopsy material. Since a solid experience in autopsy pathology is essential for the mastery of pathology, this has provided a fundamental training few other institutions offer. He likewise has made himself available for consultation and advice to his departmental colleagues. This has been done in an unhurried spirit of mutual exploration and with great wisdom and objectivity, so that the final result has reflected a combined effort in which Dr. Dawson's very profound intellectual capacities and extensive knowledge of medicine and pathology have made an important contribution. Thus, during a period of rapid growth of medical techniques and

facilities with all of the potential for turbulence and distortion, there has evolved under Dr. Dawson a department sturdily grounded in fundamentals, working cohesively and effectively, a department in which all the members have been fully aware of the depth of strength, wisdom and encouragement which their chairman has imparted.

Lee W. Wattenberg, M.D.
Minneapolis, Minnesota

Medical Men on Postage Stamps

Paul Ehrlich (1854-1915), German bacteriologist and 1908 Nobel Prize winner, was medicine's pioneer in chemotherapy: the application of chemistry to disease. He discovered the "vital stain" theory and is credited with a cure for syphilis — salvarsan or "606." For his achievements in the field of immunology along with those of his colleague, *Emil von Behring* (1854-1917), German bacteriologist and 1901 Nobel Prize winner, Germany issued a commemorative postage stamp in 1954.

Carlo Forlanini (1847-1918) was an Italian surgeon whose renown rests on his performance of the first pneumothorax operation (1892). In his memory Belgium honored him on a postage stamp issued in 1953.

It may be interesting to turn back the pages of history a few hundred years, to see what some of the really old boys had to study and stomach. Blasius Gronewalt began his medical schooling at the University of Leipzig in 1506 and in later years the books that he had used were collected by the library of Kreuzschule at Leipzig. There were only two medical books in the collection. One was the tractates and expositions of Petrus Hispanicus, who was a practising physician during the late thirteenth century, having studied at Montpellier and Paris. This book concerned treatment and dietetics and was based a great deal upon the sayings and teachings of Hippocrates (460-370 B.C.) and Galen (130-200 A.D.). The other medical book was the "Pandectae Medicinae" by Matthaeus Sylvaticus, which was a reference text of pathology and pharmacology. All of the other books were of a nonmedical nature and included texts on metaphysics, astrology, politics, ethics, economics, famous editions of Aristotle and the works of Cicero, Caesar, Plutarch, Valerius Maximus, Ovid, Livy, and Quintilian. In addition, the poor fellow had to study Greek!

— F. William Saul, M.D.: Pink Pills for Pale People

He who does not know how to manage properly a case of irritability of the stomach will never be able to treat successfully any other malady. In short, the key to a knowledge of pathology is to be found in an intimate acquaintance with gastritis and gastroenteritis.

— Francois Broussais (1772-1835)

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Curbstone Consultation

Cockroaches

QUESTION: Cockroaches, no doubt, are present throughout the world. In some areas they seem more numerous than others. (1) Are cockroaches carriers of disease? (2) Briefly, what is the best method of controlling cockroaches?

ANSWER: To the best of my knowledge, cockroaches have never been directly implicated as carriers of diseases of man. It is postulated that they could mechanically carry pathogenic bacteria in their wanderings from areas contaminated by sewage, perhaps much in the same way that flies do. However, because of their habits, they are less likely to do this than flies and, in any case, I don't know that they have ever been implicated as carriers of infectious disease. To the best of my knowledge, they do not in any other way act as direct vectors or as intermediate hosts for diseases in man.

With respect to control, the problem presents certain difficulties. As you know, cockroaches are very easily brought into the household in food packages and quickly get themselves established. They like the moist, dark places and establish their habitats in such areas. They are largely nocturnal in their habits. They usually establish themselves in areas where they have access to food. A large part of the problem in controlling them is that they drop their egg capsules in inaccessible places and these capsules often take many months to hatch. Therefore, any program of eradication would have to continue for at least six months or more. The best treatment is prevention with good sanitation and house-keeping.

The most widely used control agent, and probably the most effective one, is chlordane. This is used as a residual pesticide around baseboards and other areas where the roaches have established their runs. Spray materials are also used for their control, and of these malathion and diaznon, with or without pyrethrins, are the most effective. In years gone by, fumigation was sometimes used, but I believe that this type of treatment has been largely abandoned. Commercial establishments often engage professional pest control operators to handle the problem for them. These people will come in at regular periodic intervals to treat the infested areas.

H. H. Golz, M.D.
Corporate Medical Director
American Cyanamid Company



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and must be returned to you.

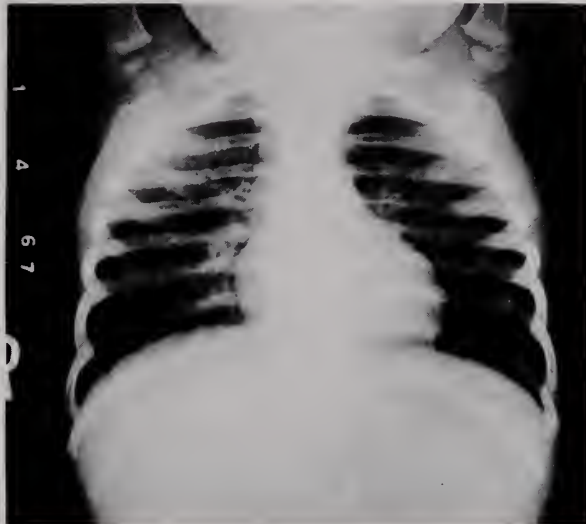
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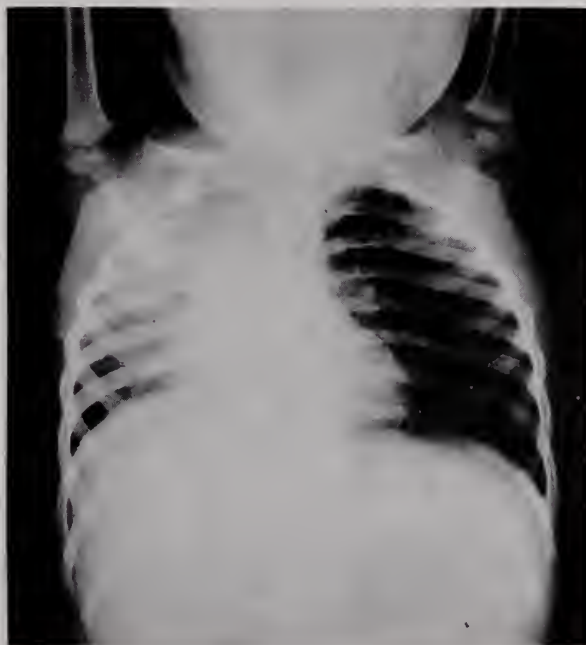
The Viewing Box

The Wheezing Child

A 17-month-old girl was admitted to Childrens Hospital because of wheezing and coughing. The past medical history was negative. On physical examination an audible wheeze was present but the infant was not in acute distress. Bilateral wheezing rhonchi, more pronounced on the left, were present. The breath sounds were diminished on the left, but there was no retraction.



Inspiration



Expiration

What is your diagnosis? (See next page.)

DIAGNOSIS: Foreign Body in the Left Main Stem Bronchus

In the above case further history revealed that the child had stumbled shortly after the mother had placed half of a shelled peanut in its mouth, and immediately developed acute wheezing and coughing. At bronchoscopy, half of a peanut was removed from the left main stem bronchus.

The most frequent cause of bronchial obstruction is bronchial inflammatory disease with partial or complete obstruction of the bronchus due to inflammatory exudate or mucus plug. Bronchial foreign bodies are a more spectacular but a less common cause of bronchial obstruction. Any child who develops a wheeze or cough after having an object in the mouth must be considered to be harboring a foreign body until proven otherwise.

A negative history regarding foreign body ingestion does not rule out this possibility in infants and children, since history is notoriously misleading in this age group.

This is a case of obstructive emphysema in which the foreign body acted as a check-valve in the left main stem bronchus allowing ingress of the inspired air but occluded the bronchus during expiration and produced obstructive emphysema.

The importance of both inspiratory and expiratory chest films is well illustrated by this case. With only a routine inspiratory film, the foreign body would have been missed. However, the expiratory film clearly revealed obstructive emphysema on the left and contralateral mediastinal shift.

Ancient Childrens Hospital Proverb: In child with wheeze, take two films (insp. and exp.) please.²

James R. Schuft, M.D.
Charles T. Miller Hospital
St. Paul, Minnesota

References

1. Caffey, John: Pediatric X-ray Diagnosis, Fourth Edition., 1961, page 287.
2. Williams, Hugh J., Childrens Hospital, Personal Communication.

Uroscopy

From time immemorial the urine has been naturally the subject of medical interest. As practiced in the 17th century it was known as Uroscopy, or "water casting." The urine, usually in a flask, was brought to the physician, who held it to the light with solemn and judicial air, while he read the patient's fate in the uplifted urinal.

"Red Urine signifieth heat of the blood; white, rawness and indigestion in the Stomach; thick, like puddle, excessive labor or sickness; white or red gravel in the bottom threatens the Stone in the Reins; black or green, commonly death."*

*Massengill, S. E.: A Sketch of Medicine and Pharmacy, S. E. Massengill Co., Bristol, Tenn.-Va., ca. 1941, p. 53.



Fracture-Trauma Conference

Motorcycle Injuries

An Analysis of 287 Victims — A Three-Year Study

IN THE LAST three years, from 1964 to 1966, a continuing study* has been conducted as to the number of injuries from motorcycle accidents seen at Methodist Hospital, Minneapolis, Minnesota, covering the five-month season — May to September. The initial results of the study were published in 1964 entitled "Motorcycle Injuries — An Increasing Traffic Problem" in MINNESOTA MEDICINE, April 1965, Gustilo et al. The study included cases that were seen at Hennepin County General Hospital.

A total of 287 victims were seen at Methodist Hospital emergency room during this three-year period. There was an increase of 23 per cent in accident victims seen in 1966 compared to 1964. Males were involved about five times more than females. The age distribution is presented in Table 1.

TABLE I

I.	Under 1	1
II.	1 to 10	6
III.	11 to 15	42
IV.	16 to 20	156
V.	21 to 25	38
VI.	26 to 30	17
VII.	Over 30	15

Of interest is the alarming number of accident victims 15 years of age or less shown in this table.

Motorcycle injuries involve primarily the extremities, resulting in fractures or ligament strains of various degrees (mild, moderate, and complete). The femur and tibia are the most frequently involved in either closed or open fracture types with occasional vascular and nerve injuries. Injuries to the brain and skull are usually fatal. The use of the helmet, however, precludes or diminishes such injuries. Therefore, the helmet is the most important single piece of equipment for a motorcycle driver. In the study of 200 patients with motorcycle injuries in 1964 at Hennepin County General Hospital and Methodist Hospital, Minneapolis, two deaths were reported, both from skull and brain injuries. Neither of the drivers wore a helmet.

*This study was supported through the St. Louis Park Medical Center Research Foundation, Minneapolis.

Continued

In the present study of 287 patients there were 26 serious head injuries. There were three deaths resulting from head injuries and helmets were not used by the victims. About 75 per cent of minor injuries are preventable, and at least 50 per cent could have been prevented with proper clothes and/or equipment.

The injuries are classified as minor or major. There were 72 major injuries and 215 minor injuries in this study. Minor trauma included simple lacerations, sprains and contusions which did not require hospitalization and which could be easily treated in the emergency room. The major category included fractures (simple, multiple, closed, and open), traumatic amputation, large lacerations, cerebral and skull injuries, and intra-abdominal injuries which necessitated either hospitalization or immediate surgical intervention. Ninety per cent of the major injuries involved the lower extremities, consisting of single or multiple fractures of the tibia, femur or pelvis.

The major injuries sustained by 72 patients are of the following types (Table 2).

TABLE 2
Types of Injuries

I. Closed fractures — 28 patients
II. Open fractures — 6 patients
III. Head injuries — 26 patients
A. Deaths — 3
IV. Chest injuries — 4
V. Spine injury — 1
VI. Miscellaneous — 19

The exact nature of these accidents can be classified into two general categories (Table 3). 1. Motorcycle upsets. 2. Motorcycle collisions.

TABLE 3
Nature of Accidents

I. Car-motorcycle collisions — 63 cases or 22%
A. Collision with turning car.
B. Head-on collision with car.
C. Collision from rear by car.
II. Upsets from various causes — 224 cases or 78%
A. Skidded on road because of no gravel.
B. Fell off for no apparent reason.
C. Lost control and turned over.
D. Accelerated too fast.
E. Collided with another motorcycle.
F. Unable to locate brake.
G. Caught fingers or feet on chains or spokes of wheels.
H. Hit immobile object fast.
I. Front wheel slipped.

The lower extremities were frequently involved with a ratio of 2:1 compared to upper extremities.

Discussion

The increasing popularity of the motorcycle both in sports riding and as a mode of transportation involves millions of Americans both young and old. It will continue to flourish and to occupy its proper place on public roads and open highways. The alarming number of victims and the severity of injuries demand public scrutiny and concern.

MOTORCYCLE INJURIES

The most common cause of accidents is improper and inadequate training of motorcycle drivers. The fact that one has a car license is not a good criterion and justification for driving a motorcycle. This light-weight machine is a potentially dangerous vehicle traveling at a very high speed. A car-motorcycle collision is the number one cause of serious injuries — commonly due to the fact that the car hits the motorcycle on the blind side in turning either left or right. Motorcycles should occupy the road just like a car and follow the rules and regulations that car drivers are required to follow.

The use of a helmet should be an absolute requirement for all motorcycle drivers.

It was alarming to note that a large number of accident victims were under 15 years of age, the majority of them passengers. A motorcycle is designed as a one-man vehicle and an additional passenger constitutes a real hazard. There are enough inherent hazards in motorcycle driving without the presence of a passenger hugging the driver.

A metropolitan-wide comprehensive study of this problem is urgently needed, particularly with regard to the licensing of motorcycle drivers and the frequency of motorcycle accidents.

Ramon B. Gustilo, M.D.
St. Louis Park, Minnesota

Acknowledgement

We thank the emergency room nurses, Methodist Hospital, for their help in this study.

Address for reprints: St. Louis Park Medical Center, 4959 Excelsior Boulevard, Minneapolis, Minnesota 55416.

Reference

1. Gustilo, Ramon B., Foss, Donald L., Leslie, William R., and Telander, Robert L.: Fracture-Trauma Conference. *Minnesota Med* 48:4:489, 1965.

Mr. Barzun Comments

Obesity

Passing from form to substance, it would seem as if our national well-being could be enhanced by a better distribution of medical efforts. Cancer is a dreadful scourge, but it seems at the moment to be nearly monopolizing talent and resources. Is the reason for this wholly disinterested and practical? Why not balance the research with a systematic review of the effects of what we take into our bodies, together with a study of our actual habits? We might learn to forestall some of our ailments as well as some of the drags on our living powers, notably that of obesity, which is a national curse. Though we live longer we do not age gracefully. Modern occupations, which are sedentary, only partly account for this: we sit and thicken, true, but that is not all there is to it. Since all foods "fatten," we must for some reason other than greed overeat. The obsession of women after thirty, of men after forty, with diets, reducers, and other means of averting the apparently inevitable cannot be called either mistaken or healthy. It seems absurd to talk of our control of nature when all we can do is use rubber bands to keep our women's shapes within bounds.

Jacques Barzun: *When the Doctor Is a Pill*
(in *God's Country and Mine*) 1954.

Metaphysics!

What is mind? No matter. What is matter? Never mind. — Thomas Key

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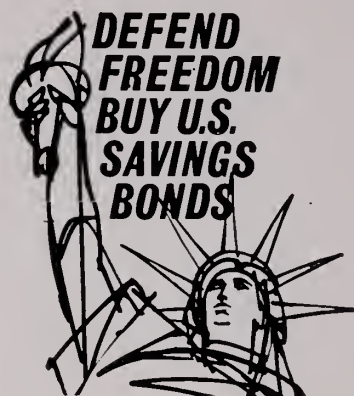
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Tumor Conference

Rupture of Bronchus

A 19-year-old Caucasian male was involved in an automobile accident. The machine he was driving left the road, striking a culvert. The patient was noted to be unconscious and in a moribund condition. Shortly thereafter he was brought by ambulance to an emergency room where a physician performed a tracheotomy. After the tracheotomy, much bloody mucus was aspirated. The patient's condition improved sufficiently to allow him to be transported to a larger hospital.

A pneumothorax was demonstrated here on a PA roentgenogram of the chest (Figure 1). An intercostal catheter was positioned and placed to suction. A vigorous air leak was noted immediately and continued for several days. Failure of closed suction prompted thoracotomy six days after injury.

At thoracotomy, a pulmonary laceration was found, and suture of the laceration was effective in controlling the air leak. The postoperative course was uneventful, and the patient left the hospital on the fifth postoperative day. An x-ray of the chest eleven days postoperatively was normal.

Fifteen days postoperatively and 26 days following the injury, the patient returned extremely short of breath. A roentgen examination of the chest at this time (Figure 2) revealed complete opacification of the right hemithorax. Bronchoscopy showed obstruction of the right main stem bronchus by what appeared to be granulation tissue. A bronchogram (Figure 3) revealed complete obstruction of the right main stem bronchus.

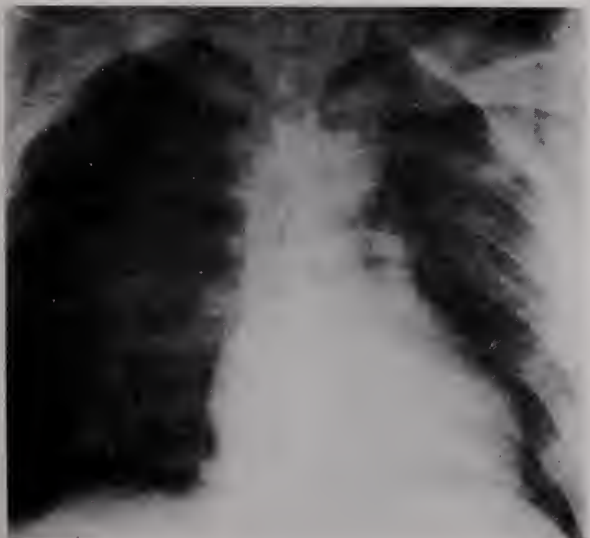


Figure 1



Figure 2

Continued



Figure 3

A second thoracotomy was performed 26 days after the injury, and detailed dissection of the pulmonary hilum was carried out. A bronchial laceration with incomplete separation of the cut ends of the bronchus was found. This was repaired by resection of the fibrotic ends and re-anastomosis using 3-0 chromic sutures. The postoperative course was uneventful. Postoperative roentgenograms of the chest and a bronchogram revealed satisfactory reconstruction and healing (Figure 4). The patient remains asymptomatic.

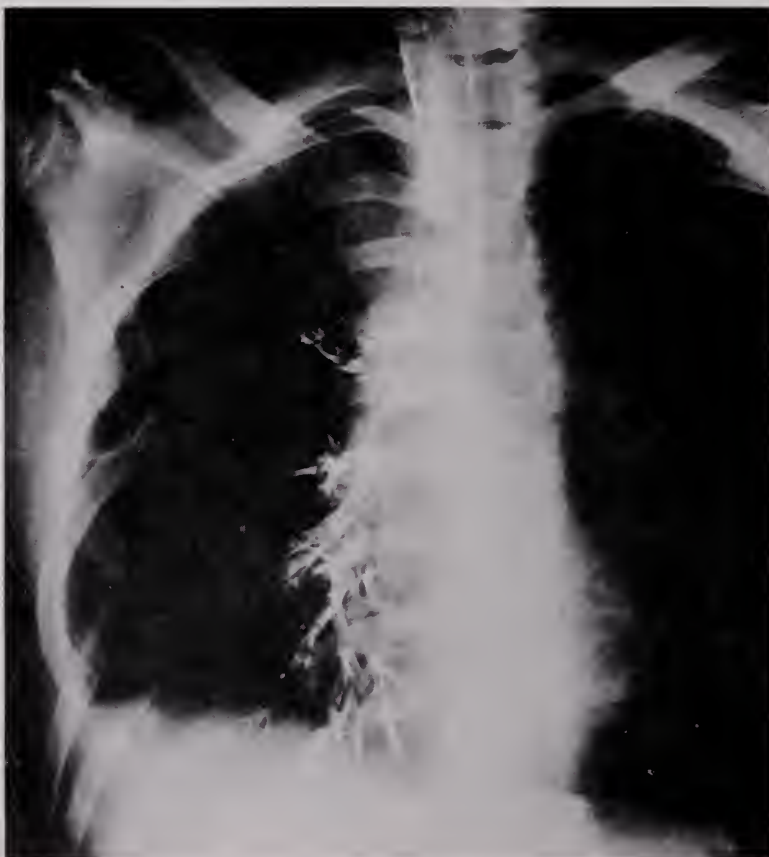


Figure 4

Discussion

Bronchial rupture or injury must be suspected in all serious thoracic trauma. Unexplained persistence of pneumothorax, despite intercostal suction, coupled with expectoration of bloody mucus, is a clue which should alert the examiner to the possibility of a bronchial rupture. Air passage in and out of the involved lung can occur for a period of weeks after the injury, provided the tear is incomplete. Persistent atelectasis or pneumonia is an additional clue suggesting a diagnosis of injured bronchus.

Recent surgical advances in the field of lung transplantation and extensive bronchial resections for malignancy have yielded valuable experience in the field of bronchial reconstructive surgery. Excellent results can be expected if the diagnosis of bronchial rupture is made. Post-operative pulmonary studies demonstrate satisfactory function of the reconstructed segments.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Petrus Hispanus

In his Commentaries Petrus Hispanus (c. 1215-1277), self-styled "professor of the art of medicine and investigator of the truth," revealed his empirical bent by posing such provocative questions as:

Can natural death be retarded?

How can animals who eat poisons be food for men?

Why is man less hairy and of weaker constitution than the brutes?

Why are animals soft in infancy and fruits hard?

Should paralytics eat fried fish?

Why is oil best at the top, honey at the bottom, wine in the middle of the cask?

What part of water is more truly water: top, bottom, or middle?

Why are pigs' intestines the best of animals that walk and geese's intestines of those that fly?

Is human milk subtler than asses' milk?

If the spleen causes laughter by purifying the blood, why isn't love caused by the gall-bladder?

Is raw cheese better than cooked, and solid cheese or cheese with holes in it?

Why are fools so fond of cheese?

Why does human urine enrich vines?

Are apples good in fevers?

Why pepper is good for dimmed eyes?

Remedies Derived from Living Creatures Remedies Derived from the Elephant

The blood of the elephant, the male in particular, arrests all those defluxions known by the name of "rheumatismi." By the touch of an elephant's trunk, head-ache is alleviated, if the animal happens to sneeze at the time more particularly. The right side of the trunk, attached to the body with red earth of Lemnos, acts powerfully as an aphrodisiac. Elephant's blood is good for consumption, and the liver for epilepsy.

— Pliny

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Medical Seminar

Mushroom Poisoning (Mycetismus)

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FOR CENTURIES the mushroom has served both as a source of food and as a source of psychic stimulation for religious and tribal orgies. Ancient Babylonians and early Romans considered the mushroom a delicacy and on many occasions, historians tell us, mushroom poisoning took its toll. The earliest record of such poisoning was in the fifth century B.C., when it was reported that the wife and three children of the Greek poet Euripides died from mushroom poisoning.¹ The historian Pliny has referred to these early years as "The Golden Age of Poisoning" largely because of the effects of the mushroom.²

The first fatality reported in the United States was in 1871.³ Since that time few deaths from mushroom poisoning have occurred in this country, the latest figures showing 36 fatalities from 1924 to 1965.⁴ Deaths from mushroom poisoning account for less than 2% of all fatalities recorded from poison control centers throughout the country.⁵ At the Mayo Clinic no deaths from mushroom poisoning or reports of patients made seriously ill from the mushroom are on record. A similar situation exists for Minnesota, according to Dr. Warren Lawson, Supervisor of the State of Minnesota Poison Information Center.⁶ Paradoxically, the rarity of mushroom poisoning in the United States seems to be one of its dangerous features, as both its symptomatology and the treatment of its effects are easily forgotten. In contrast, however, the problem in Europe is a major one, the difference probably being due to the more avid mushroom hunters in European countries. In

Germany alone, for example, it is estimated that 200 people die each year from mushroom poisoning.⁴

More than 3,000 different types of mushrooms are known, and of these, 70 to 80 are known to be toxic to man. Apparently there is great variability in individual susceptibility to mushroom poisoning, and there seems to be a similar variability in toxicity among the mushrooms themselves. Some are toxic only if eaten in large quantities, at specific stages of maturity or during certain seasons, or if eaten in the cooked or raw form. Most authors agree that most deaths (90%) are caused by the genus *Amanita* and in particular the *Amanita phalloides*.² Only toxins of the *A. phalloides* or its phenotypes* produce parenchymatous necrosis in man. A large part of the remaining toxic mushrooms probably could be more accurately described as indigestible, as they produce only transient, unpleasant gastrointestinal effects. Buck⁷ has reviewed the 24 fatal cases of mushroom poisoning reported in the American literature as of 1961 and noted the following etiologic agents: *A. phalloides* and *A. verna* (11 cases); *A. pantherina* (1 case); *Gyromitra esculenta* (7 cases); and undetermined species (5 cases).

Amanita Muscaria (Fly Agaric)

This is one of the largest and most colorful mushroom. At times it reaches heights of 12 inches, with caps six to 10 inches in diameter, the color of the cap varying from orange to yellow to white, with the reddish shades predominating. The color, however,

*See Test Your Word Score Page 521.

Continued

changes with the environment and age of the plant and seems to fade in direct sunlight, in rain, or with aging⁸ (Figure 1). This mushroom is commonly called the fly agaric, actually receiving its name from the common house fly, *Musca domestica*, to which it is extremely toxic. *A. muscaria* is found east of the Great Plains, particularly in the upper lake states under the pine and aspen trees and in the Pacific Northwest in forested areas. Closely related to *A. muscaria* is the mushroom *A. pantherina*, which is most frequently involved in muscarinic poisoning in the Pacific Northwest.

Although rarely causing fatalities, *A. muscaria* produces toxic symptoms, which are due either to mass stimulation of the postganglionic parasympathetic fibers or to stimulation of the central nervous system. In addition, symptoms suggestive of atropine toxicity have been noted. Thus, symptoms of intoxication are threefold and depend essentially on the relative amounts of the

three recognized toxic substances present.⁹ The amounts of these substances vary from mushroom to mushroom and even vary within the same mushroom from season to season.

Muscarine

This was one of the first cholinergic drugs to be systematically studied and was first separated in a rather impure form in 1868 by Schmiedeberg and Koppe.¹⁰ It is a quaternary amine, with structural and physiologic similarities to acetylcholine. Muscarine stimulates the postganglionic parasympathetic fiber in a manner similar to that of acetylcholine. In very large doses, muscarine also may stimulate the autonomic ganglia; but these effects are far overshadowed by its effects on glandular tissue and smooth muscle. No effect on skeletal muscle has been noted. Muscarine is 143 times more potent than acetylcholine although the onset of action is much slower. The increased potency of muscarine is most likely due to its resistance to breakdown by cholinesterases. Muscarine is heat stable and hence not appreciably altered by boiling. Its effects are rapidly counteracted by atropine.

Pilzatropin (Mushroom Atropine)

Soon after the isolation of muscarine it was found that an incompletely purified preparation of *A. muscaria* from the Bavarian Alps caused cardio-acceleration, a change inconsistent with the usual muscarine effects. This "impurity" was named pilzatropin by Kobert in 1891, and its chemical structure and paper chromatographic pattern were found similar to those of L-hyoscyamine, a racemic form of atropine.⁷

Pilztoxin

Although not definitively identified, a third toxin called pilztoxin is believed to exist in *A. muscaria*.⁷ Its presence is suggested because of certain manifestations of the central nervous system that persist in both man and animal after neutralization of muscarine. These manifestations are narcotic-like intoxication, convulsions, hallucina-

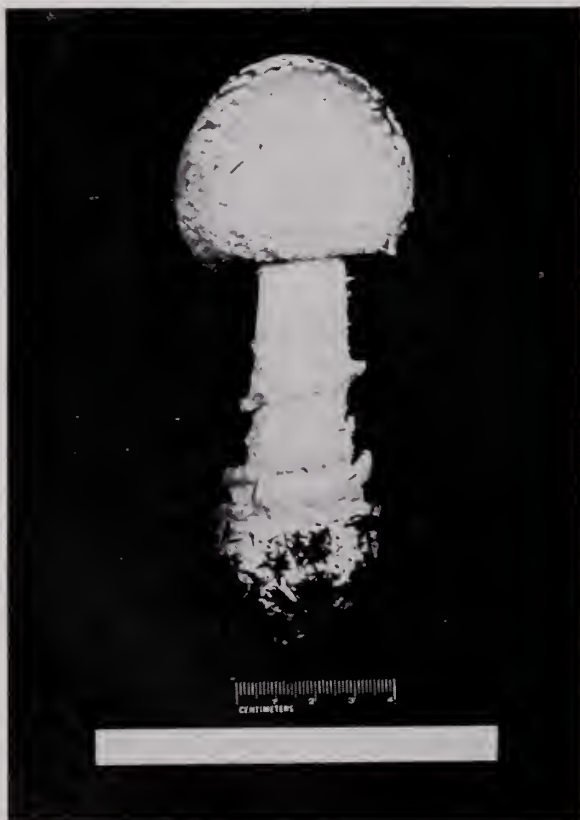


Fig. 1 — *Amanita muscaria*. (Reproduced with permission from Smith, A. H.: The Mushroom Hunter's Field Guide. Ann Arbor, University of Michigan Press, 1963, 264 pp.)

tions, and occasionally death.

Amanita Phalloides (Death Cap)

A. phalloides and its phenotype *A. verna* are extremely toxic mushrooms found commonly throughout the north temperate zones in America and Europe. Enough poison is contained in a piece of one mushroom to be fatal to man (Figure 2).¹¹

Experimental work on the *A. phalloides* toxin began in 1793 when Paulet discovered that the toxic element was not destroyed by drying or by heat. The toxin itself was first isolated in 1937 by Lynen and Wieland and was called phalloidin.¹² Subsequent to this, four other toxic fractions have been separated, and these may be conveniently classified as phalloin, alpha amanitine, beta amanitine, and gamma amanitine.¹³ Each toxin seems to be a cyclic, sulfur-containing peptide that depends on the integrity of the sulfur atom for its toxic effects. The alpha-amanitine fraction is largely responsible for the toxic effects of the mushroom. Apparently, the toxins are quickly bound to albumin and then "fixed" to the parenchymal cells, thus leading to the necrosis of these cells. Necrosis is particularly evident in the liver, kidney, and brain.

Classification of Mushroom Poisoning

The first and probably still the best classification of mushroom poisoning was set forth in 1923 by Ford,¹⁴ who divided mushroom poisoning into five groups, the division being made according to the predominant clinical features: (1) mycetismus gastrointestinalis, (2) mycetismus sanguinarius, (3) mycetismus nervosus, (4) mycetismus cholericiformis, and (5) mycetismus cerebralis.

Mycetismus Gastrointestinalis

This is a mild illness predominantly of nausea, vomiting, mild abdominal discomfort, and diarrhea. It may be so mild as to occur without note, or at times it may be moderately severe and require medical attention. Symptoms of central nervous system dysfunction are not present, and likewise parasympathetic symptoms in organs other than the gastrointestinal tract are not prominent.

This illness usually terminates spontaneously, and the patient is restored to good health in one or two days. Various mushrooms have been implicated in this type of poisoning, but no fatalities have been reported.

Mycetismus Sanguinarius

This is a relatively rare illness brought on by the eating of *Helvella esculenta* or beefsteak morel, a mushroom found in the upper Great Lakes region; this type of mushroom is toxic to some persons but not to others. Its toxicity is mediated by helvellic acid, a heat-resistant hemolytic poison. Gastrointestinal symptoms are present at the onset and are followed by rapid hemolysis associated with transient hemoglobinuria and mild jaundice. The prognosis is good although fatalities have occurred. Autopsies show widespread pigmentation of liver, kidney, and spleen secondary to the hemolysis.



Fig. 2 — *Amanita phalloides*. Note convex cap with grayish brown center. (Reproduced with permission from Christensen, C. M.: Common Edible Mushrooms. Minneapolis, University of Minnesota Press, 1943, 124 pp.)

Continued

Mycetismus Nervosus (Rapid Type)

This is the poisoning caused by *A. muscaria*, *A. pantherina*, and other less common fungi such as *Clitocybe sudorifica*, *Inocybe infida*, and *A. crenulata*. Symptoms are due to the massive postganglionic, parasympathetic stimulation by muscarine. They begin from a few minutes to three hours after ingestion and initially present as violent gastrointestinal cramping with nausea, vomiting, and watery stools, followed by or associated with increased salivation, lacrimation, sweating, miosis, bronchoconstriction, an asthmatic type of dyspnea, a slow pulse, and at times shock. The pupillary response to light and accommodation may be decreased or absent, and there may be confusion, vertigo, convulsions, and coma. In some cases, psychic symptoms may be present and may even predominate. These are characterized by anxiety, hallucination, manic symptoms, dancing, singing, or a furious tremor. In general, these psychic symptoms pass in several hours and are followed by a period of somnolence. Although the majority of patients recover completely, a few may become comatose and die. The mortality rate in this general category of poisoning is extremely low, primarily because of the early onset of symptoms and hence the earlier treatment. Atropine is the treatment of choice and quickly abates the muscarinic symptoms, no matter if they are mild or severe. If death is to occur, it usually does so within the first hour.

Mycetismus Choleriformis (Delayed Type)

The deadly *A. phalloides* and *A. verna* are the responsible agents in this type of poisoning. In contrast to the rapid type of mycetismus nervosus mycetismus choleriformis involves symptoms of delayed onset, six to 15 hours after ingestion. The clinical picture presents in three phases. Initially, there is the explosive onset of severe abdominal pain, nausea, vomiting, watery diarrhea, melena, and severe dehydration with extreme thirst. This is believed to represent a direct irritative effect of the toxin on the gastrointestinal mucosa, although a muscarinic component may be present. Death may occasion-

ally occur during this initial stage, although usually the patient is seen soon enough and supportive therapy begun so as to prevent this. There may then occur a period of "false remission" wherein the patient's symptoms partially clear for a variable length of time, characteristically followed by worsening of the abdominal pains and then varying degrees of deterioration in hepatic, renal, and neurologic functions. The liver enlarges and becomes tender, and jaundice is noted along with abnormal findings on liver-function studies. Often there is a period of hyperglycemia followed by a more persistent hypoglycemia. This alteration in glucose metabolism is believed to be of hepatic origin. Pathologically the liver shows a generalized loss of architecture and massive areas of hemorrhagic necrosis. Renal involvement is clinically manifest as acute renal failure and, as with most similar cases, oliguria occurs and is followed in three to 17 days by diuresis. Deteriorating renal function is manifest by uremia, electrolyte and pH abnormalities, hematuria, and proteinuria. Pathologically, there is necrosis of both distal and proximal convoluted tubules but little involvement of the glomeruli. Electron microscopic studies have revealed enlargement of the mitochondria in the tubular cells and disruption of their membranes and cristae.¹⁵ Central nervous symptoms are varied, usually appear terminally, and are indicative of diffuse cerebral involvement. There may be somnolence, confusion, coma, convulsions, increased intracranial pressure, involuntary movements, and vasomotor collapse. Examination may reveal rigidity, tremor, hyperactive reflexes, bilateral Babinski's sign, ocular palsies, and on occasion meningeal signs. In addition, peripheral manifestations such as motor and sensory changes in the extremities are sometimes noted. Although a cursory pathologic study of the brain in *A. phalloides* poisoning was carried out in 1855 by Maschka, the first and most complete study was that of Marcovitz and Alpers in 1935.¹⁶ Prior to this time the manifestations of the central nervous system were attributed solely to hepatorenal failure, which was invariably present. These authors,¹⁶ however, demonstrated def-

MUSHROOM POISONING

inite pathologic alterations in the brain, consisting of marked cerebral and meningeal edema, degeneration and loss of pyramidal cells, areas of necrosis of white and gray matter, punctate cortical and brain stem hemorrhages, and toxic changes in the glial elements. Numerous investigators have since substantiated these findings. In addition to these pathologic changes, toxicity from *A. phalloides* is often associated with increased capillary fragility that leads to petechiae, retinal hemorrhages, and serosanguineous pleuritis, as manifested by a positive Rumpel-Leede test.* There may also be hemorrhagic necrosis of the myocardium.

The usual course of this disease is six to eight days in adults and three to four days in children. The mortality rate is high, estimated to be 50 to 90%. At times, 100% of those afflicted die, despite good supportive care.

Mycetismus Cerebralis (Psychotropic Mushrooms)

This classification was initially utilized by Ford¹⁴ to include symptoms produced by mushrooms of the genus *Panaeolus*. Symptoms consisted of transient exhilaration, immoderate laughter, peculiar visual disturbances, and staggering. These symptoms started four to five hours after the fungi were eaten and persisted for 24 to 48 hours. Other psychotropic mushrooms may be placed in this category because they produce symptoms similar to those just described.

A psychotropic agent is by definition any compound that produces psychotic phenomena in the presence of a clear sensorium. Psilocybin is one such drug and was isolated by Hofmann from the hallucinogenic mushrooms.^{17,18} It is a phosphorylated indole that is structurally related to serotonin and reserpine.

In three regions of the world men continue to eat mushrooms for their psychic effects. The *A. muscaria* is eaten in Siberia; in New Guinea certain tribes eat a mushroom called Nodda in preparation for battle or in times of sorrow or excitement; and in Mexico certain cults eat and worship

the *Psilocybe mexicana* and have done so since the time of Montezuma in 1502.

In a study of 22 volunteers at the Mayo Clinic¹⁹ psilocybin was noted to produce the following symptoms: initially, light-headedness, euphoria, anxiety, perioral paresthesia, blurred vision, increased vividness of visual images and colors, and increased auditory perception; first hour, dreamy state, euphoria, uncontrollable laughter, hallucinations of colored pattern with eyes closed; second hour, slowed passage of time, feelings of unreality and depersonalization, flashes of introspection, increased somatic perceptions; fourth hour, gradual waning of symptoms; and fifth hour, total resolution.

After total resolution there were no general side effects, although some reported an overwhelming fatigue and depression that persisted for 24 hours.

Disulfiram-Containing Mushrooms

Reports of toxicity due to the "inky caps" have appeared in the files of the State of Minnesota Health Department.⁶ Inky-cap mushrooms belong to the genus *Coprinus* and are given their name because of their black spores. In general, these are edible mushrooms. However, if alcohol is drunk within 24 hours after the mushroom has been eaten, toxic symptoms occur, which come on within minutes to two hours after the alcohol has been consumed and are identical with those produced by disulfiram (Antabuse). There may be flushing of the face, a feeling of warmth, a metallic taste in the mouth, hyperventilation, nausea, vomiting, sweating and tachycardia, and paresthesia. These symptoms are transient, usually clearing spontaneously. At times a severe reaction to disulfiram or acetaldehyde may occur, characterized by congestive heart failure, myocardial infarction, cardiac arrhythmias, respiratory distress, and convulsions. In 1956 disulfiram was isolated from these mushrooms by Simandl and Franc.²⁰

Treatment

In the majority of cases other than those due to *A. muscaria* and *A. phalloides* symp-

Continued

*See Test Your Word Score Page 521.

toms subside spontaneously without treatment. It is ideal for the attending physician to obtain parts of the offending mushroom for identification. However, this is not always possible as the mushrooms have usually been completely eaten, and even if recoverable their accurate identification is difficult. Pieces or spores may be recovered from the gastric aspirate, and at times these may serve as a source of identification. However, the physician's decision for treatment depends entirely upon the patient's history and symptoms. The most important consideration in the differential diagnosis is that between poisoning from *A. phalloides* or *A. muscaria*. In this regard, the time of onset is of great value. Poisoning with both types begins with explosive gastrointestinal symptoms; but in *A. muscaria* poisoning these occur within minutes to three hours after ingestion, whereas in *A. phalloides* poisoning their onset is delayed from six to 15 hours after ingestion. There is a suggested treatment for specific types of mushroom poisoning.

Atropine

A. muscaria or *A. pantherina*: Atropine is the treatment of choice and gives excellent results when both mild and severe symptoms are present. The dose is 0.6 mg. and may be repeated in one hour. Gastric lavage should be attempted, as this removes undigested mushrooms, and sedation with phenothiazines or barbiturates is useful when states of excitement or psychic symptoms are present.

Gastric Lavage

A. phalloides or *A. verna*: No specific antidote is available for this type of poisoning. Gastric lavage may be useful as late as 48 hours after ingestion; however, its value is questioned by some because the late onset of symptoms permits the fungi to pass well beyond the stomach. Instead, a vigorous catharsis seems more realistic and at times has been lifesaving. Atropine is of value, as the initial, explosive gastrointestinal symptoms may have a muscarinic character. Opiates can be given to relieve pain.

Intravenous Fluid

Intravenous feedings with glucose and electrolyte replacement should be initiated early because many of these patients are badly dehydrated and have lost electrolytes by vomiting and diarrhea. In addition, the alteration in glucose metabolism with initial hyperglycemia and the subsequent, more persistent hypoglycemia must be corrected, because the seizures that occur probably have a hypoglycemic basis.

Diet should be restricted to fruit juices, soups, tea, and sugar for at least 24 hours. The relatively high carbohydrate content of this diet is beneficial in the presence of hepatic involvement and is less irritating to an already irritated gastric mucosa.

Treatment of renal failure must include adequate hydration initially to distinguish between oliguria that is secondary to dehydration alone and that due to renal failure. If no response in urine volume occurs with hydration, there is probably renal tubular necrosis. If this is true, care must be taken not to overhydrate the patient. A daily intake of 400 ml. plus losses is recommended. Electrolyte imbalance, particularly hyperkalemia, should be noted and accurately corrected. Adequate amounts of glucose (150 to 200 gm./day) should be administered to minimize protein breakdown and hence potassium elevation.

Renal Dialysis

The value of renal dialysis has recently been discussed^{15,21} and seems to be of value in some cases. Elliott and associates²¹ described a case of mushroom poisoning in which successful treatment with hemodialysis was carried out. Myler and co-workers¹⁵ described two patients with *A. phalloides* toxicity who were treated with intermittent peritoneal dialysis; one patient survived, but the other died. The surviving patient was oliguric for 30 days and was treated with two 4-day courses of peritoneal dialysis. *Amanita* toxins are quickly bound to susceptible parenchymal cells. This fact plus the large size of the phalloidin or phalloin molecule makes the toxins poorly dialyzable. Therefore, successful use of dialysis has not

MUSHROOM POISONING

been attributable to removal of the toxin per se but instead to a supportive role during temporary periods of renal failure. Myler and associates¹⁵ considered intermittent peritoneal dialysis to be more desirable than hemodialysis, although it is a much slower process. Peritoneal dialysis allows for a simultaneous adjustment of electrolytes and glucose, whereas hemodialysis does not. Also, the large molecule of the toxin passes more easily through the peritoneal membrane than through the cellophane membrane of the hemodialysis apparatus.

Other Treatments

In the treatment of poisoning associated with myocardial involvement, digitalis is used.

Another technique includes the use of sensitized rabbit stomach and brain. In 1932 Limousin and Petit¹ noted that rabbits died of phalloidin toxin when the agent was given parenterally but not when it was given orally. Rabbits then were "sensitized" with orally administered phalloidin. Minced

rabbit stomach plus raw rabbit brain was then given to cats. This mixture seemed to protect the cats against poisoning. Similar attempts were carried out with humans who received various proportions of sensitized rabbit stomach and rabbit brain. To date this has been ineffective and not used in this country.

Antiserum has been used by some. Rabbits and horses were sensitized with progressively increasing doses of toxin, and their serums were found to have antitoxic qualities. This antiserum has been highly acclaimed in the French literature although it is believed by most in this country to be of limited value. Antibodies to *A. phalloides* have never been demonstrated.

To relieve the symptoms incurred from psychotropic mushroom poisoning, chlorpromazine hydrochloride is effective.

Transfusion helps hemolytic mushroom poisoning. In poisoning from disulfiram-containing mushrooms, treatment is necessary only for the severe reactions, in which cases oxygen inhalation and orally administered ephedrine are of value.

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References

1. Grossman, C. M., and Malbin, B.: Mushroom Poisoning: A Review of the Literature and Report of Two Cases Caused by a Previously Undescribed Species. *Ann Intern Med* 40:249, 1954.
2. Vander Veer, J. B., and Farley, D. L.: Mushroom Poisoning (Mycetismus): Report of Four Cases. *Arch Intern Med* 55:773, 1935.
3. Abdul-Haj, S. K., Ewald, R. A., and Kazyak, Leo: Fatal Mushroom Poisoning: Report of a Case Confirmed by Toxicologic Analysis of Tissue. *New Engl J Med* 269:223, 1963.
4. Harrison, D. C., Coggins, C. H., Welland, F. H., and Nelson, Sherwin: Mushroom Poisoning in Five Patients. *Amer J Med* 38:787, 1965.
5. Cann, H. M., and Verhulst, H. L.: Mushroom Poisoning. *Amer J Dis Child* 101:128, 1961.
6. Lawson, W.: Personal communication to the author.
7. Buck, R. W.: Mushroom Toxins: A Brief Review of the Literature. *New Engl J Med* 265:681, 1961.
8. Smith, A. H.: The Mushroom Hunter's Field Guide. Ann Arbor, Univ Mich Press, 1963, 264 pp.
9. Buck, R. W.: Toxicity of *Amanita Muscaria*. *JAMA* 185:663, 1963.
10. Schmiedeberg, and Koppe: Cited by Bowden, K., and Mogey, G. A.: The Story of Muscarine. *J Pharm Pharmacol* 10:145, 1958.
11. Christensen, C. M.: Common Edible Mushrooms. Minneapolis, Univ Minn Press, 124 p, 1943.
12. Wieland, T., and Wieland, O.: Chemistry and Toxicology of the Toxins of *Amanita Phalloides*. *Pharmacol Rev* 11:87, 1959.
13. Wieland, O.: Changes in Liver Metabolism Induced by the Poisons of *Amanita Phalloides*. *Clin Chem* 11:323, 1965.
14. Ford, W. W.: A New Classification of Mycetismus (Mushroom Poisoning). *Trans Ass Amer Physicians* 38:225, 1923.
- 15-21 May be secured from the author or the reprints.

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Treating the Patient Who Has Convulsions*

PATIENTS WHO suffer from convulsive disorders far outnumber other types of neurological patients. The estimate that one out of every fifty humans will have some form of seizure disorder during his lifetime is probably conservative. Convulsive disorder patients come to medical practitioners in numbers which exceed the much more publicized "stroke" patients. It is also true that for each one who comes under medical care for this disorder there are others who go undiagnosed and still others who go to great lengths to hide the fact that they have the disorder even from their physicians. It is definitely the most common disorder of the central nervous system of man.

For several decades now the medical practitioner has had innumerable books and articles available to him on the subject of convulsive disorders. The more subtle forms of focal motor, sensory and visual seizures have been described, classified and then described further. Psychomotor or limbic lobe seizures have been widely publicized for the past fifteen years. There remain few if any doctors who are unaware of the etiological possibilities for this malady; certainly all are aware of the role of brain tumors. The anticonvulsants have not been neglected; literature has fought to describe the newer ones sometimes even before the pills "have dried." Full-page advertisements and "detail" men have publicized the merits of products with most convincing scientific proof, usually in chart form. The diagnosis and treatment of the convulsive disorder has probably been covered "too well" in recent times and the "treatment of the *patient* with a convulsive disorder" discussed not at all.

The usual patients with seizures are those who do not have brain tumors or a "long-named" central nervous system degeneration. Most frequently they have had their peculiar paroxysms recurrently from early life due to a "scar" on their brain from an infection or trauma. Many have gone weeks to years between seizures, only to have them recur. The treatment of this group is not always easy and those who endeavor to do a good job of it find no help in the literature on the common problem of recurrent seizure activity.

The difficulty arises in most seizure patients shortly after they have been diagnosed and placed on anticonvulsants. They then proceed to have another convulsion. At first the physician confidently increases the dosage of the anticonvulsant or changes to another agent. After a variable period of time the patient again has another convulsion. This pattern often continues until toxic doses of anticonvulsants are being used. Both the physician and the patient are discouraged by the result. Consequently many physicians "give up" trying to treat these patients, and many a patient discontinues treatment because its effects are worse than the disease.

*Presented at the Black Hills Medical Seminar, August 5, 1966.

Continued

The basic fact that anticonvulsants are effective and remain so even when a seizure breaks through must be remembered; no tolerance or loss of potency of their medicine occurs in the seizure patient. A "therapeutic regime" is the amount of medication that a patient may take with benefit but which does not interfere with his usual activity. "Therapeutic regime" does not mean an amount of medication that causes over-sedation, diplopia, ataxia or inebriation. Maximum anticonvulsant benefit in the treatment of major seizures can usually be achieved by the administration of diphenylhydantoin (Dilantin) 300 mg. per day, mephobarbital (Mebaral) 300 mg. per day, and primidone (Mysoline) 750 mg. per day in total dosage or in varied and lesser amounts. Once this level is achieved and the patient returns, after having had another seizure, what can the physician do?

When this patient reports another seizure do not reach for the prescription pad; instead, inquire about a few general factors that often influence seizure activity. These are fatigue, infection, changes in medication, toxins and hydration.

Very often a patient who has been well controlled for weeks or months and then has a seizure does so because of an infection. The common cold, an otitis, a pharyngitis, a bout of "flu" or any other infection may be the cause of the difficulty, and a history regarding infections must be taken in this type of patient. Frequently the patient has continued his usual activity, admitting only to "feeling miserable" and to having "kept working", but with an obvious infectious process. The lowering of the seizure threshold by an infectious process is to be expected, and when the infection is cured there is no need to increase the anticonvulsants. It is far wiser to treat the next minor infection vigorously with bed rest and appropriate agents so that the convulsive disorder does not "break through" a second time.

Equally as often, when a patient develops recurrent seizures for no apparent reason, the cause will be fatigue. The socioeconomic stresses and the difficulty of getting and holding a good job frequently force these patients to work long hours or at two jobs in order to support themselves and their families. This results in less than adequate sleep, and chronic fatigue results, producing many "supposed" treatment failures. Fatigue occurs on another basis as well. Socioeconomic stress frequently results in considerable marital discord and anxiety in seizure patients and many suffer from insomnia, resulting in poor seizure control due to chronic fatigue. In none of these patients will increasing the anticonvulsants counteract the fatigue and be of benefit. The only way to reduce fatigue is to rest. Rest does more to fortify the brain's own physiological deterrents to seizure activity than even anticonvulsants, and to achieve optimum seizure control every patient must have eight hours of sleep every night!! If sleep is lost for one night due to an emergency it must be "made up" at the earliest possible moment. During a state of fatigue seizure control is precarious.

A surprising number of patients who return to the physician with complaints of seizures do so because they have failed to take the medications or have reduced or discontinued them. They usually fail also to volunteer this information for obvious reasons: a point that must not be forgotten. These seizure patients often have a poor understanding of

the convulsive state; many feel they have the evil "biblical epilepsy" and society still treats them this way. They frequently try to deny their malady by decreasing or discontinuing their medications: the most concrete method of denial. A discussion of a "scar on their brain" and its need for continued medication is most necessary.

Another group of patients who return with recurring seizures while taking adequate medication is not quite so clear-cut. This includes a number of female patients who tend to have an aggravation of their seizures prior to or during the menses and who do not benefit from increased amounts of anticonvulsants. The value of diuretics in this group suggests that their fluid balance may in some way be involved and indicates a good method of treatment. The condition is never severe enough to necessitate oophorectomy. Others in this group develop recurrent seizures only after bouts of excessive drinking, usually alcoholic. The period of the "hang-over" and of excessive thirst is a period of seizure aggravation. Optimal seizure control is not possible in patients who persist in bouts of very heavy drinking. The socioeconomic stresses of the seizure patient are often so great that they foster alcoholism, which only compounds the problem; therefore it is wise to strongly discourage alcoholic consumption in seizure patients.

Emotional stress, anger, fear, sorrow or shock do not account for seizure aggravation, except when they result in chronic fatigue of the patient. The physiologic need of the brain for adequate rest plays an important role in convulsive activity, and stress frequently interferes with adequate rest.

To successfully treat the patient with a convulsive disorder requires the judicious use of drugs below sedating levels and close attention to general factors that play an important role in clinical aggravation: namely, fatigue, infection, and auto-regulation of medicine and alcohol.

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Minneapolis, Minnesota

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St. Luke's Hospital Seminar

St. Luke's Hospital, St. Paul, is presenting a seminar entitled "Clinical Aspects of Hematology" on April 27, 1967, starting at 1:30 p.m., in the St. Luke's Hospital auditorium. The featured speaker will be Dr. A. J. Quick of Marquette University Medical School. Contact: C. E. Turbak, M.D. at St. Luke's Hospital.

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A combined dinner-meeting of the Hennepin County Medical Society will be held, May 1, at the Pick-Nicollet Hotel. Dinner at 7:00.

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Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

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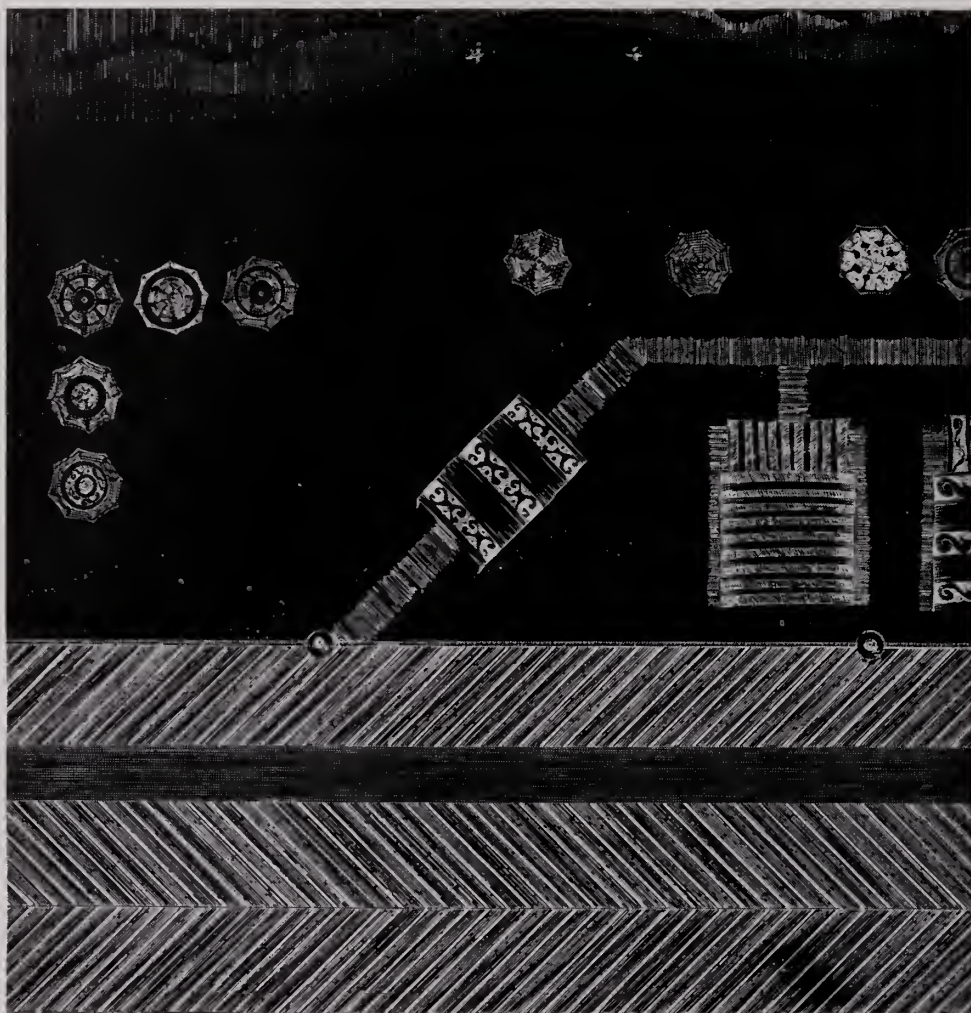
Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), onophyloxia, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.



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Bacteremia Due to Gram-Negative Bacilli

Some Current Concepts. Part II*

Supportive Therapy

CONSIDERABLE CONTROVERSY exists regarding ancillary management of these infections, especially in regard to antishock regimens, but the measures that are frequently employed are mentioned at least for the sake of completeness. Although any outline of therapy is controversial, different regimens are being employed in several medical centers and comparative data will become available. At the outset, it should be recalled that differences in animal species, especially those between the canine and human, in their reactions to endotoxin, make it extremely difficult to relate experimental data to clinical phenomena in a precise manner. Use of various agents to improve blood flow and tissue perfusion in bacteremic shock cannot be directed by generalization but depends upon precise identification of hemodynamic derangements present in the individual patient.

Important among supportive measures is the management of fluid and electrolyte deficits. Although parenteral glucose appears to prolong life in experimental animals, overadministration of fluids, especially of saline, during oliguria can embarrass cardiac function and induce pulmonary edema. Of course, if hypovolemia is present in the case at hand, it should be corrected. Measurement of central venous pressure indicates the competence of the heart to accept and expel a given blood volume and may serve as a guide to volume repletion. Fluid can be cautiously given as long as the central venous pressure is low or normal, that is, 5 to 15 cm. of water.

Replacement of blood may be required in

such patients as those having bleeding lesions of the gastrointestinal tract or underlying hematologic disease. In these patients it is conceivable that reduced blood volume predisposes them to the development of shock from bacteremia due to endotoxin-producing gram-negative bacilli as is suggested in certain animal experiments.

Antiacidotic measures are being investigated, and while acidosis can be corrected by infusion of sodium bicarbonate, levels of blood lactate appear to be uninfluenced unless peripheral circulation is improved concurrently. Use of other buffering agents in patients having lacticacidosis, such as tris (hydroxymethyl) aminomethane or THAM, may have application in the future. An isotonic solution of THAM (36 Gm. in 1,000 ml.) may be given intravenously during one- to two-hour periods. A possible means of lowering blood levels of lactic acid may be the administration of 5% carbon dioxide in oxygen. Also there are experimental data that one may reduce lacticacidemia by administration of dihydroxyacetone, a product of glucose metabolism which transforms lactic acid into pyruvic acid.

The gallbladder, postoperative wounds, obstructive uropathy, and so forth may constitute nidi of infection from which the blood is reseeded with organisms, and surgery may be required. One attempts to control the bacteremia before subjecting the patient to added stress, but sometimes bacteremia persists until such a nidus is attacked surgically. Metastatic suppuration requiring surgical attention most often complicates *Bacteroides* bacteremia.

Vasopressors have been used in an attempt to restore circulating homeostasis by rein-

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*Read at the meeting of the American Academy of General Practice, Lake Okoboji, Iowa, June 18, 1966.
See Part I, Minnesota Med 50:397, 1967.

forcing the natural bodily reaction to prevent so-called irreversible shock, and also to forestall renal ischemia and renal shutdown. Use of a vasopressor is a temporary supportive measure until other therapeutic procedures and the patient's own compensatory mechanisms are able to maintain adequate blood pressure and tissue perfusion. Of the numerous vasopressor agents available, those which have been used most commonly in the recent past are metaraminol, levarterenol, and angiotensin. Of course, a current question is whether vasodilators should be used rather than vasopressors.

Prior to the discussion of vasoactive drugs, it may be well to review some of the terminology currently employed in describing these agents and their actions. There are two types of adrenergic receptors situated in the vascular system: alpha and beta. Alpha-adrenergic receptors mediate vasoconstrictor responses while beta receptors mediate vasodilatation. Thus, levarterenol may cause vasoconstriction by stimulating alpha receptors in blood vessels, while isoproterenol may cause vasodilatation by stimulating beta receptors. In addition, both levarterenol and isoproterenol may cause positive chronotropic effects (increased cardiac rate) and positive inotropic effects (increased myocardial contractility) via their action on the heart. Alpha-adrenergic blockers (alpha-receptor blockers), which may antagonize vasoconstrictor effects, are exemplified by phenoxybenzamine and phentolamine.

Metaraminol (Aramine) can be given intramuscularly, but preferably is given intravenously, in amounts of 100 to 250 mg. in 500 to 1,000 ml. of fluid. Experimental data suggest that the release of levarterenol from sympathetic nerves has a major part in the action of metaraminol. Therefore, when refractoriness to metaraminol is suspected, one substitutes levarterenol. Reserpine may deplete bodily stores of levarterenol, with consequent reduced response to metaraminol.

Levarterenol or norepinephrine (Levophed) is given intravenously in increments of 4 ml. of a 0.2% solution in 1,000 ml. of 5% dextrose in distilled water at a rate sufficient to maintain the desired blood pressure.

Fluids containing dextrose protect against loss of levarterenol's potency due to oxidation; levarterenol should not be given in saline solution alone. More than a dozen ampules have been given in one day to patients who remain hypotensive. Use of leg veins in patients with arterial disease and use of hand veins are avoided, and the site of infusion and the course of the vein infused are observed for local ischemia. If blanching occurs, necrosis is minimized on stopping the infusion and infiltrating the area with adrenergic blocking agents such as phentolamine or piperoxan. Protection against local necrosis may follow addition of 5 to 10 mg. of phentolamine or of 10 to 20 mg. of heparin to each liter of solution containing the agent. Levarterenol and metaraminol increase peripheral resistance and stimulate the myocardium. In contradistinction to the reaction in normal subjects, in patients who are in shock administration of these drugs tends to increase cardiac output.

Angiotensin (Hypertensin) has maintained the blood pressure satisfactorily during bacteremic shock. Although angiotensin has been given intramuscularly, usually it is given intravenously. A vial of angiotensin contains 2.5 mg. of the drug, and one to four vials are added to 500 to 1,000 ml. of fluid; as many as 10 vials have been given in a 24-hour period. Angiotensin directly increases peripheral resistance without affecting the heart; the action of angiotensin appears to be independent of adrenergic receptors. Patients not responding to levarterenol have responded to angiotensin, but since the converse also occurs, in some patients a trial of both drugs is required.

A Y-tube apparatus used to give a vasopressor intravenously allows its periodic discontinuation so that only the minimum is consumed, and yet it is immediately available if hypotension occurs. Similar titration is not possible with vasopressors given intramuscularly. When vasopressors are given, it is unnecessary to raise the systolic blood pressure above 100 mm. of mercury in a previously normotensive patient.

As aforementioned, vasodilators, including alpha-adrenergic blocking agents,¹³ are being

investigated in place of vasopressors in patients having bacteremic shock. Proponents of their use point out that pallor, sweating, and tachycardia reflect vasoconstriction, and these workers discourage administration of vasopressor drugs because of concern that a further reduction in systemic blood flow might result. They postulate that dilatation of blood vessels rather than their further constriction by vasopressors is required to relieve visceral pooling. These workers have concluded that the body's attempt to preserve blood supply to vital centers such as the heart and brain at the expense of other areas is undesirable; they consequently give a vasodilator to undo the reaction. Some of these workers emphasize that this intensified vasoconstriction may be responsible for decreasing renal blood flow and urinary output; but if over-all measures do not correct the underlying cause of the shock, increased urinary output, as an isolated achievement, is less than a therapeutic triumph. Phenoxybenzamine (Dibenzylamine) administered intravenously in amounts of 1 mg. per kg. of body weight is commonly recommended by these investigators; but this form of the drug is not commercially available. Although use of phenoxybenzamine may increase the urinary output, it may also further reduce the blood pressure and require administration of blood or its products or a plasma expander to combat the increased hypotension. For this reason, it is recommended that vasodilators be used only when effective circulating blood volume is known to be normal or is being replaced.¹⁴ Some workers recommend administration of a vasodilator when there is increased central venous pressure, decreased cardiac output, and pulmonary congestion; but these findings also might be interpreted as indications for digitalization. Despite considerable discussion based on animal experimentation, there are little data on the efficacy of alpha-adrenergic blocking agents in the management of human victims of bacteremic shock. Eckenhoof and Cooperman¹⁵ gave phenoxybenzamine to 24 patients, six of whom died; excessive vasodilatation was considered a contributory factor in the deaths of five of these six patients. Phentol-

amine (Regitine) is also an alpha-adrenergic blocking agent which has been employed for its vasodilating effect.

Isoproterenol (Isuprel) is chemically related to epinephrine and levarterenol and, as aforementioned, is a so-called beta-receptor stimulator. The drug is used in cardiogenic shock and is currently being reevaluated in bacteremic shock.¹⁶ Unlike its chemical relatives, isoproterenol may induce peripheral vasodilatation. Monitoring of cardiac rhythm is advised during administration of the drug since arrhythmias may result from its inotropic effect. Isoproterenol is given intravenously in an initial dose of 2.5 mg. in 500 ml. of 5% dextrose in water at a rate of 0.5 to 1 ml. per minute. If no reaction occurs within 15 minutes, the rate of infusion is doubled.

Other vasodilators that have been recommended include trimethaphan (Arfonad) and hydralazine (Apresoline).¹⁴

There is some reticence to abandon the use of vasopressors because evidence exists that the mortality rate is less for patients having bacteremic shock who receive vasoconstrictor drugs. Hall and Gold¹⁷ reported a mortality rate of 57% for 21 patients who received no vasopressor drugs and 36% for 14 patients who were given these agents. Hodgkin and Sanford¹⁸ in their more recent study also concluded that use of vasopressor agents was of value in bacteremic shock. A possible basis for the discrepancy in opinions regarding the use of vasopressors is that less than desirable results have been noted in patients who have reached stage II of shock. In an attempt to reconcile the data at hand and to provide a temporary scheme, enabling one to make a clinical decision regarding the use of vasoactive drugs in a given instance, the following generalizations may be helpful until more concrete data are available. Vasopressor drugs may be employable in patients with bacteremic shock when blood volume deficit is safely excluded as the cause of shock. If the patient does not respond to such management after a reasonable interval, use of a drug such as isoproterenol may be considered. However, it

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should be emphasized that one must guard against losing valuable therapeutic time while procuring multiple electrocardiograms, awaiting the results of elaborate laboratory procedures, and belatedly diagnosing bacteremic shock when the patient has not responded to regimens more pertinent to noninfectious shock. If bacteremic shock is not diagnosed early and if adequate antibiotic therapy is not quickly initiated, no supportive treatment, including use of vasopressors or vasodilators, will have optimal effect.

Oxygen therapy tries to counteract tissue anoxia due to reduced arterial blood flow, and although it is helpful in experimental animals, the logic of its clinical use is disputed. Hyperbaric oxygenation also has prolonged life in experimental animals. High-pressure oxygen therapy may increase oxygen transport to the tissues and also have a bacteriostatic effect on the infecting bacilli. A major objection to the clinical use of hyperbaric oxygenation is the possibility of fatal oxygen toxicity involving the pulmonary and central nervous systems.

An airway is provided if necessary.

Digitalization of the hypotensive patient is carried out only if the central venous pressure remains above 15 cm. of water and particularly if other evidences of heart failure, such as pulmonary edema, are detected. Digitalization can be carried out by giving 0.5 to 1 mg. (2 to 4 ml.) of digoxin intravenously and then 0.25 mg. every two to four hours; full digitalization may be achieved after a total of 1 to 1.5 mg. is given. It is to be recalled that in human bacteremic shock many of the affected patients are elderly and their cardiac function may be compromised by coronary atherosclerosis and other types of heart disease.

Such mechanical measures as elevating the foot of the patient's bed and applying an abdominal binder and leg bandages may increase venous return and cardiac output. However, there are no exact data indicating that these measures are of substantial benefit.

The exact application of hypothermia¹⁹ in bacteremic shock remains unclear although

it has been helpful in experimental animals. The rationale for hypothermia is based on reduction of the need for cellular oxygenation, thereby favorably influencing the metabolic environment. If hypothermia is not used, the patient is kept comfortably warm; but overheating, which may dilate superficial vessels and further increase the capacity of the vascular bed, is avoided.

In cases wherein hypotension is prolonged, renal shutdown may occur. Usually recovery from renal shutdown is heralded by reappearance of excretory function within 10 to 12 days. However, excretory function reappears before regulatory function, and death with progressive azotemia and acidosis remains possible. Hemodialysis has contributed to maintaining life and reducing morbidity during the oliguric phase of renal shutdown. It should not be reserved as a last desperate measure, since its failure to prevent death may reflect belated use. In this same regard, there are data indicating that renal failure which is partial or incipient may be reversed by the use of mannitol intravenously. Significant diuresis is an average increment in urine flow of more than 0.2 ml. per minute in three hours after 25 gm. of mannitol is given intravenously. If less than 50 ml. of urine is produced in the next two hours, no more mannitol should be given. The mechanism of mannitol diuresis appears to be acute expansion of blood volume with subsequent increase in glomerular filtration rate. Lack of significant diuresis after administration of mannitol usually indicates fully developed renal shutdown. Mannitol may produce transient vacuolization of the proximal tubules, but this does not appear to be associated with changes in renal function and therefore is not considered significant. It is advised that concentrates of mannitol not be given in the presence of hyponatremia or hypochloremia; their use also is inadvisable in the presence of congestive heart failure.

Use of morphine, meperidine (demerol), barbiturates, and other depressants is best avoided.

Use of adrenal glucocorticoids has been advocated despite the fact that these pa-

tients, even when moribund, show no abnormality of the secretory function of the adrenal gland.^{20,21} Some investigators oppose administration of vasopressors on the basis that the adrenal glands are capable of providing these in sufficient quantity; but contrariwise, some of these workers give massive doses of adrenal glucocorticoids despite no evidence of adrenal insufficiency. On reviewing mortality rates in reported series wherein steroids were used, one might conclude that patients receiving them have a higher mortality rate. McCabe and Jackson² concluded that the effects of adrenal glucocorticoids in their patients were adverse. Known complications of steroid therapy include impairment of the immune response and an increased susceptibility to upper gastrointestinal bleeding; the latter complication can lead to considerable diagnostic and therapeutic confusion. Such bleeding occurs spontaneously in victims of bacteremic shock and may be potentiated by steroids. An additional objection to the use of such therapy is that, on analysis of the causes of death in patients having bacteremic shock due to gram-negative bacilli and given adrenal glucocorticoids, a complicating staphylococcal superinfection is not uncommon. My colleagues and I have limited administration of adrenal glucocorticoids in nonpharmacologic dosage to those patients who were receiving them prior to the onset of bacteremia.

Also, we have not used blood or its products in the definitive management of this complication because in the usual case of bacteremic shock there appears to be no decrease in blood volume but rather stagnation and faulty redistribution of it. It is recognized, of course, that replacement of blood may be required in such patients as those having bleeding lesions of the gastrointestinal tract or underlying hematologic diseases. On the other hand, a rapid intravenous infusion of 500 ml. of low molecular weight dextran,²² in patients with a normal central venous pressure but low cardiac output and hypotension, appears to be relatively safe and may normalize the circulatory dynamics without resorting to a vasopressor or a vasodilator. Depending on individual circum-

stances, the dextran has been given over periods ranging from 30 to 120 minutes; 500 ml. can be administered slowly over subsequent 12-hour periods. Low molecular weight dextran (40,000) is available only for investigation in the United States; the molecular weight of dextran usually employed in this country is 75,000. Higher molecular weight dextrans (110,000 and up) are also being employed by some investigators. Normally, dextran 40 is excreted in one to two hours, but in shock its excretion may be prolonged to four hours or longer. Administration of the agent may increase cardiac output, decrease peripheral resistance, and restore urinary output.

Heparinization to counteract intravascular coagulation during experimental bacterial shock has been advocated, but its benefit also lacks clinical confirmation. Numerous other regimens, including testosterone, aldosterone, serotonin antagonists, chlorpromazine, and even antihistaminics, have been described as being helpful in experimental animals, but this does not automatically assure their efficacy in the human subject.

Overemphasis of a unitarian concept of shock with insufficient attention to etiologic differences may lead to regimens largely based on wishful thinking. At this time, there is no one regimen equally applicable to such diverse etiologic entities as cardiogenic, hemorrhagic, and bacteremic shock. Cardiac support and replacement of blood do not influence the basic defect in the usual case of bacteremic shock, and these and other symptomatic procedures are designed only to maintain the patient's life until antibiotic therapy can control the overwhelming infection which is the essential cause of his vascular collapse. It is appreciated, of course, that patients with such underlying conditions as coronary artery disease and bleeding lesions of the gastrointestinal tract may require special attention in this regard, but these isolated requirements hardly justify universal administration of digitalis and blood. When there is a diagnostic and therapeutic difficulty, as exemplified by the patient with underlying hematologic disease in

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whom shock suddenly develops, monitoring of the central venous pressure and determination of the hematocrit value may aid one in deciding about the advisability of blood replacement. If in such a patient, on administration of blood, the central venous pressure rises abruptly, the transfusion can be stopped and phlebotomy carried out by the same route, that is, the central venous catheter. Consequently, it is possible to act in an empiric manner and yet undo potential harm before it has become catastrophic. When an investigator states that he employed antibiotics in the management of bacteremic shock, it would be helpful for comparative analysis if he were to make clear the dosage and duration of such therapy, as well as the specific drugs employed, and perhaps most importantly the time consumed between the onset of infection and the initiation of antibiotic therapy. If antibiotic therapy is inadequate, the essential cause of bacteremic shock is not being combated, and consequently therapeutic success is unlikely.

Prognosis

The prognosis is considerably determined by the nature and severity of the initial lesion, the presence of underlying disease, prior therapy, the duration of the infection before institution of appropriate management, and complications such as bacteremic shock, metastatic infection, and superinfection.

Patients who recover usually have had the benefit of early diagnosis and treatment. Since the commonest precipitant of bacteremia is urethral manipulation, including catheterization, such "potential candidates" must be recognized and managed accordingly to assure the best prognosis. Along with monitoring of the candidate's temperature and pulse rate, hourly determinations of the blood pressure and recording of the urinary output appear to be the best routine objective indices of his current status.

In our experience, the majority of deaths have occurred in cases of serious associated conditions, and in at least 50% of fatalities the associated condition was responsible. In this regard, one should be prepared to encounter the potential paradox that as man's

ability to prolong life improves, his success in the management of bacteremia due to gram-negative bacilli may decrease. This is so because the underlying disease predisposing to infection may so diminish host resistance that recovery is virtually impossible, at least within the present limits of therapy.

Summary and Conclusions

Only about 10% of the cases of bacteremia due to gram-negative bacilli occur in the absence of underlying disease, therapy capable of altering host resistance to infection, or precipitating operation or instrumentation. In managing any patient with possible predisposing disease or treatment — especially a patient with disease of, or recent operation on, the urinary or gastrointestinal tract who has fever — one should be constantly aware of the possible presence or supervision of bacteremia and, consequently, bacteremic shock due to gram-negative bacilli.

Empiric antibiotic therapy is begun when report of cultures is received or, in seriously ill patients, after blood is drawn for cultures. If the patient's condition and microbiologic data later indicate such empiric therapy to be unsatisfactory, it is modified accordingly. Use of specific antibiotics in the initial management of gram-negative bacteremia is only theoretically possible because, practically, one is often thwarted by lack of cultural proof of the pathogen and, almost always, of its in-vitro susceptibilities. In little more than one third of our cases did the usual circumstances surrounding such infections, including the intrinsic delay in the reporting of in-vitro bacterial susceptibilities, allow use of a single drug. However, these difficulties are not of such magnitude that one cannot devise adequate antibiotic therapy on an empiric basis. If such a regimen is not employed, or not employed early in the infection, the essential problem is not being attacked and recovery is unlikely.

To the present, the majority of our patients having bacteremic shock have received a vasopressor, most commonly levarterenol, and antibiotic therapy; they have not received steroids as definitive therapy. Since the mortality rate in patients, managed in

this manner, is lower than has been reported in certain series in which other regimens were employed, members of our group plan to continue management of bacteremic shock in this manner, at least until sufficient data are available which would make a change in therapy reasonable. At the same time, we are continuing our evaluation of cephalothin-colistin (or cephalothin-poly-myxin B) as empiric antibiotic therapy, isoproterenol (Isuprel) as an antihypotensive agent, and the rapid infusion of dextran in place of a vasoactive drug in selected patients. Perhaps more important than the investigation of new regimens is the recognition of the potential candidate and the monitoring of his temperature, blood pressure, and urinary output, so that early diagnosis and treatment of the complication are possible. It is our experience, too, that when stage II of shock has been reached, optimal response to therapy, including vasopressor therapy, is less likely. Such factors as blood loss and impaired cardiac function undoubtedly play a part in individual cases of bacteremic shock, and in such cases, therapy

should encompass these considerations, but this does not appear to be a reasonable basis for recommending that these therapeutic facets be generally applied.

In conclusion, there appear to be several possible explanations for the rather marked differences in mortality rates of various series of patients having bacteremia and bacteremic shock due to gram-negative bacilli, and consequently for the controversies regarding management of these infections. These include (1) delayed diagnosis with consequent failure to initiate pertinent treatment early in the process, (2) inappropriate antibacterial therapy, (3) the type of patient concerned, since those with serious underlying diseases are less likely to recover, (4) reliance on experimental data which may not be applicable to the human subject, (5) overemphasis of a unitarian concept of shock with insufficient attention to the particular cause of infectious shock, and (6) attempts at supportive therapy which may be of questionable value or perhaps actually militate against host defenses.

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References

- 1-12 Printed with Part I. See Minnesota Med 50: 397, 1967.
13. Nickerson, M.: Factors of Vasoconstriction and Vasodilation in Shock. J Mich Med Soc 54:45, 1955.
14. Webb, W. R.: Vasodilators in Shock — When? Southern Med J 59:257, 1966.
15. Ekenhoff, J. E., and Cooperman, L. H.: The Clinical Application of Phenoxybenzamine in Shock and Vasoconstrictive States. Surg Gynec Obstet 121:483, 1965.
16. Kardos, G. G.: Isoproterenol in the Treatment of Shock due to Bacteremia With Gram-Negative Pathogens. New Engl J Med 274:868, 1966.
17. Hall, W. H., and Gold, D.: Shock Associated With Bacteremia: Review of 35 Cases. Arch Intern Med (Chicago) 96:403, 1955.
18. Hodgins, U. G., and Sanford, J. P.: Gram-Negative Rod Bacteremia: An Analysis of 100 Cases. Amer J Med 39:952, 1965.
19. Allen, J. M., Estes, J. T., and Mansberger, A. R., Jr.: The Use of Hypothermia in Septic Shock. Amer Surg 26:11, 1960.
20. Melby, J. C., and Spink, W. W.: Comparative Studies on Adrenal Cortical Function and Cortisol Metabolism in Healthy Adults and in Patients With Shock due to Infection. J Clin Invest 37:1791, 1958.
21. Melby, J. C., Egdahl, R. H., and Spink, W. W.: Secretion and Metabolism of Cortisol After Injection of Endotoxin. J Lab Clin Med 56:50, 1960.
22. Cohn, J. N., and Luria, M. H.: Studies in Clinical Shock and Hypotension. III. Comparative Effects of Vasopressor Drugs and Dextran. Arch Intern Med (Chicago) 116:562, 1965.

They Say

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Not indicated in children under 6 years; absolute dosage for 6 to 12 year-olds not established.

Side Effects: Therapy-interrupting side effects are rare. Transient mild drowsiness is common initially; if persistent, reduce dosage. Dizziness, vertigo and headache have also occurred infrequently; syncope, rarely. Mild paradoxical reactions (excitement, stimulation of affect) are reported in psychiatric patients. Minor diffuse rashes (morbilliform, urticarial and maculopapular) are rare. Nausea, lethargy, edema, slurred speech, tremor and altered libido are rare and generally controllable by dosage reduction. Although rare, leukopenia and hepatic dysfunction including jaundice have been reported during therapy. Periodic blood counts and liver function tests are advised. Ataxia, reported rarely, does not appear related to dose or age.

These side reactions, noted with related compounds, are not yet reported: paradoxical excitation with severe rage reactions, hallucinations, menstrual irregularities, change in EEG pattern, blood dyscrasias (including agranulocytosis), blurred vision, diplopia, incontinence, stupor, disorientation, fever, euphoria and dysmetria.

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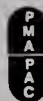
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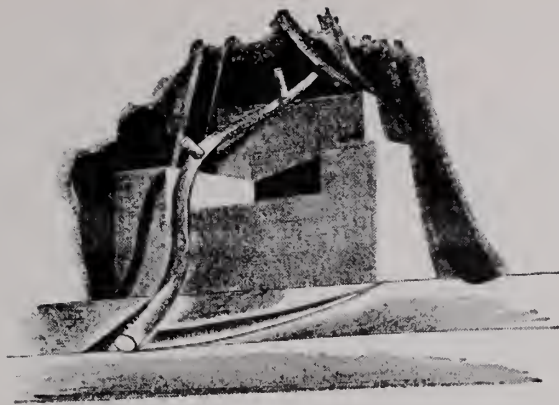
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In Memoriam

It is impossible that anything so natural, so necessary, and so universal as death, should ever have been designed by Providence as an evil to mankind. — Swift

ARNOLD LARSON, M.D.

Dr. Arnold Larson, 73, a resident of Detroit Lakes for thirty-eight years and a practicing physician and surgeon for thirty-six years, died January 25. Born in Fillmore County, Dr. Larson received degrees at both the University of Minnesota and the University of Pennsylvania.

He was a member of the Clay-Becker County Medical Society and the American Medical Association. He was a Life Member of the Minnesota State Medical Association and an active member of the Kiwanis Club and Masonic Lodge.

Dr. Larson is survived by his son and two daughters.

JOHN PETER FREEMAN, M.D.

Dr. John Freeman, 90, a lifetime resident of Glenville, died February 2. A practicing doctor since 1900, Dr. Freeman retired in 1960. He was a graduate of the University of Illinois Medical School.

Dr. Freeman was a member of the Freeborn County Medical Society and the American Medical Association and a Life and 50 Club Member of the Minnesota State Medical Association.

He is survived by his wife, a son and a daughter.

JESSE P. NEHRING, M.D.

Dr. Jesse Nehring, 63, Preston physician, died January 25. A native of Belgrade, Dr. Nehring graduated from the University of Minnesota Medical School in 1929 and immediately went to Preston where he practiced medicine for thirty-eight years.

He was the Fillmore County coroner, county public health officer and medical examiner for the Selective Service. Dr. Nehring was a member of the National Academy of General Practitioners, the Zumbro Valley Medical Society, the American Medical Association, the Minnesota Academy of General Practitioners, the Southeastern Minnesota Medical Society, and the Minnesota State Medical Association.

He is survived by his wife, three daughters and a son, Dr. John D. Nehring of Wabasha.

RAYMOND T. HEALY, M.D.

Dr. Raymond T. Healy, 83, family physician in Pierz for fifty-five years, died February 14. Born in LeSueur, Dr. Healy received his medical degree from the University of Minnesota. He served for one year on the State Board of Health in Minneapolis and went to Pierz in 1912. Pierz honored him on his 50th year in that community, and Healy Junior High School was named in his honor.

He served on the medical staff of St. Gabriel's hospital, Little Falls, was a member of the Upper Mississippi Medical Society and the American Medical Association. He was a Life and 50 Club Member of the Minnesota State Medical Association.

He is survived by his wife and two daughters.

JOHN A. WINTER, M.D.

Dr. John A. Winter, 87, an eye, ear, nose and throat specialist in Duluth, died February 15. Born in Nagaunee, Michigan, Dr. Winter graduated from the University of Michigan in 1902. Four years later he entered Johns Hopkins Medical School where he studied under the famed Sir William Osler. Serving his internship in Chicago, Dr. Winter practiced for two years in Calumet, Michigan, before journeying to the University of Vienna in Austria to advance his education in his specialty.

A year later he returned to the Illinois Charitable Eye and Ear Infirmary in Chicago. In 1910 he went to Duluth and launched his practice. Dr. Winter and his seven colleagues established the Duluth Clinic in 1915.

He was a member of the St. Louis County Medical Society, American Medical Association, Minnesota Academy of Ophthalmology, American College of Surgeons and the American Academy of Ophthalmology and Otolaryngology. Dr. Winter was a 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by two nieces and two nephews.

Regardless of Mother's Opposition

I had always wanted to be a doctor like my father before me. The story goes that I came into the house one day when I was about six and announced that when I grew up I was going to be a big fat doctor. Mother just shook her head. She knew only too well the wearisome toil, the long hours with broken sleep, the heavy responsibilities, and the sheafs of unpaid bills that play so large a part in a doctor's life. Father knew these things, too; he never encouraged me or discouraged me.

One day when I was thirteen and we were alone in the office, I told Father that I had fully made up my mind to be a doctor regardless of Mother's opposition. He listened to what I had to say in grave silence, eyeing me thoughtfully over his glasses.

"All right. I'll take you along with me to-morrow," he said.

So the next morning I drove him to the home of an old gentleman I knew well whom I had always seen wearing a long white beard. When I saw him with his beard shaved off and a big, repulsive looking epithelioma protruding from his lower lip, I admit I was shocked. While another doctor administered the anaesthetic my father removed the cancer and the entire lower lip with it. The sight of the old gentleman's mutilated face, covered with blood, exposing a few old snags of teeth, gurgling and bubbling as he breathed, was not a pretty one. I must have behaved well, however, for Father seemed satisfied. It may be he was trying to test me.

A short time after that Father took me ten miles into the country to drive for him, badly in need of the doze he could get in the buggy on the way. When we arrived at the farmhouse we found that the farmer had a strangulated hernia. An immediate operation was required and there was no other doctor available to give the anaesthetic. So I was pressed into service. The operation went smoothly and I was thrilled and delighted. But now I began to think I was well on the way to becoming a doctor myself. From that day on it was settled. Mother's opposition subsided and finally ceased.

Urling C. Coe (1881-)
in *WHY WE BECAME DOCTORS*
edited by Noah Fabricant, M.D., 1954

Ed. Note: Urling Coe enjoyed a successful practice in Portland, Oregon.

Whatever theory we adopt respecting the foundation of the social union, there is a circle round every human being which no government ought to be permitted to overstep; there is a part of the life of every person of years of discretion within which the individuality of that person ought to reign uncontrolled either by any other individual or by the public collectively. Scarcely any degree of utility short of absolute necessity will justify prohibitory regulation, unless it can also be made to recommend itself to the general conscience. — John Stuart Mill



Grand Rounds

*Ethacrynic Acid, A Potent Diuretic**

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Medical Resident

THE MANAGEMENT OF patients with fluid retention has steadily improved. Probably the largest single factor responsible for this improvement has been the use of increasingly effective diuretics. The four major categories of diuretics which act on renal tubular transport systems are (1) organic mercurials, (2) chloruretic sulfonamides (thiazide derivatives), (3) sulfonamides that inhibit carbonic anhydrase, and (4) aldosterone antagonists. A new chemical class of diuretics was introduced in 1962.¹ This new class was the α and β unsaturated ketone derivatives of aryloxyacetic acid. Structural variations were studied and one of the potent compounds included a chloride substituted aromatic nucleus with a terminal methylene group. This compound is known as ethacrynic acid or MK-595 and is currently produced by Merck Sharp and Dohme under the trade name of Edecrin. This paper will discuss the chemical and pharmacologic aspects of the drug as well as its clinical application in fluid retention in hepatic, cardiovascular, and renal disease.

Absorption, Distribution and Excretion

Ethacrynic acid is chemically unrelated to other diuretic agents. It is sparingly soluble in water but its sodium salt is soluble in water and stable at body pH.² The drug is readily absorbed from the gastrointestinal tract.³ The clearance of ethacrynic acid is dependent upon glomerular filtration rate and both renal tubular secretion and reabsorption. By using C¹⁴-labeled ethacrynic acid in dogs, Beyer and others⁴ show that the drug was transported in the proximal tubules. Secretion occurs in the proximal portion of the nephron with back diffusion in the distal nephron. It

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, August 16, 1966.

Continued

was also shown that secretion was inhibited by Probenicid on a competitive basis and by denitrophenol on a metabolic basis. Intravenous administration of labeled ethacrynic acid in dogs showed 20 to 35% recovery in the urine within 24 hours, and 25 to 50% of the drug recovered in feces within 24 to 48 hours.⁴ Four hours after intravenous injection, 12 to 30% of the dose can be recovered in bile.⁴ Thus the liver is directly involved in the metabolism of ethacrynic acid. Elimination over a seven-day period showed less than 0.5% in exhaled CO₂ and the rest recovered in urine and feces. Thirty to 40% of the drug remains unchanged in the urine; 40% was recovered as ethylacetate and 20 to 30% as a cysteine adduct. Ethacrynic acid is not dialyzable from the tissue.

Mode of Action as a Diuretic

Ethacrynic acid acts directly on the kidneys. On a histochemical basis this drug is similar in action to the mercurial diuretics. Both agents reduce the concentration of stainable protein-bound sulfhydryl groups in renal cells.^{4,5,6,30} It is thought that this reaction interferes with the sulfhydryl catalyzed enzyme systems of the renal cells involved in absorption and secretion of electrolytes leading to a saluresis and diuresis.

Site of Action

There have been a number of studies involving animals and normal individuals in an attempt to demonstrate the diuretic effect of ethacrynic acid and to localize its site of action in the kidney.^{4,7-15,35} Figure 1 will serve as a review of renal physiology needed to understand the mechanism of action of ethacrynic acid. The reabsorption of solute, sodium and chloride occurs in both the proximal and distal portions of the nephron. Proximal reabsorption of solute is accomplished with isosmotic* amounts of water. Approximately two thirds of the filtered sodium and water is reabsorbed in isotonic proportions in the proximal tubule. The remaining filtrate is acted upon distally, two sites being the ascending limb of the loop of Henle and the distal tubule. In the ascending limb sodium is actively reabsorbed in greater proportion to water, entering the medulla to maintain a hypertonic state (counter-current mechanism).¹⁶ Final urine concentration is accomplished by passive movement of free water from the collecting ducts under the control of antidiuretic hormone into the hypertonic medulla. Therefore the ascending limb of the loop of Henle is indirectly involved with the mechanism of final urine concentration. The second site of sodium reabsorption is in the distal tubule. Here sodium may or may not be absorbed isosmotically, but this site is not related to the counter-current mechanism.

Three definitions involving renal hydrodynamics are in order:

1. Osmolar clearance: That volume of water necessary to contain the urinary solutes in a solution isosmotic with plasma.
2. Free water clearance: The excess or deficit of water beyond the osmolar clearance. In a state of water diuresis this value is positive, and during antidiuresis, this value is negative.
3. Free water reabsorption: That volume of reabsorbed solute-free water occurring in the collecting ducts.

A diuretic acting solely on the proximal tubule, inhibiting sodium and chloride reabsorption, during maintained water diuresis, would increase

*See Test Your Word Score Page 521.

urine volume, osmolar clearance and free water clearance. This occurs because of the increased urine flow as well as the increased amount of solute present in the urine to be acted upon by the distal sites of sodium reabsorption. A diuretic acting solely on the distal sites of absorption would produce little change in urine flow, an increase in osmolar clearance, and a decrease in free water clearance under a state of maintained water diuresis. Cannon and others^{7,8} showed that in normal individuals during maintained water diuresis (forced oral and intravenous fluids) ethacrynic acid produced an increase in osmolar clearance and urine volume and a decrease in free water clearance. The authors proposed that the site of action of this drug involved both the proximal and distal sites of sodium and chloride reabsorption, but that the proximal site was more prominent. Goldberg and others⁹ studied the renal hydrodynamics in a similar way but included work involving conditions of hydropenia (withholding fluids), at which time antidiuretic hormone would have its maximal effect. They pointed out that diuretics acting primarily on the proximal tubules would cause an increase in free water reabsorption because of the availability of more osmotically active solute for transport into the medulla, i.e., the ascending limb of the loop of Henle. The authors demonstrated that under the condition of hydropenia, normal individuals showed a decrease in free water reabsorption following ethacrynic acid. After the effects of ethacrynic acid were manifested by a fall in the free water reabsorption, the addition of an osmotic diuretic (Mannitol) did not significantly raise the free water reabsorption. When an increased quantity of sodium was presented to the loop of Henle, active transport into the medulla was blocked. No diuretic before ethacrynic acid has been shown to lower the free water clearance during water diuresis and lower the free water reabsorption during hydropenia. The authors suggest

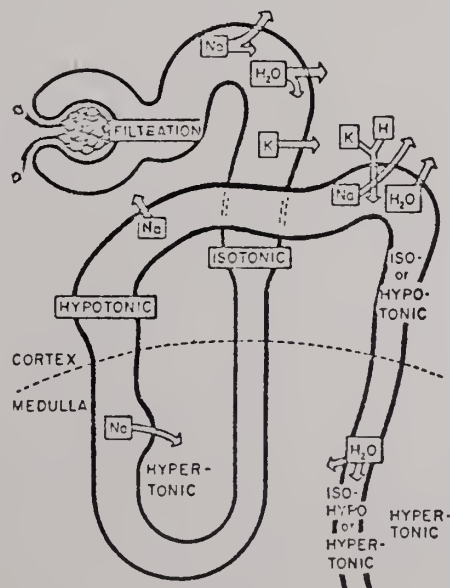


Fig. 1 — Simplified diagram of the nephron. See text.

*From Gantt, Proceedings of the Symposium, Austin, Texas. The Role of Endocrinology and Diuretics in Hypertension and Edema. Excreta Med Foundation, December, 1965.

Continued

the site of action of this drug to be at the ascending limb of the loop of Henle, a site at which inhibition of sodium and chloride reabsorption would fulfill the above requirements.

Process of Dilution and Concentration

Thus ethacrynic acid has a definite effect on renal processes of dilution and concentration resulting from primarily a sodium and chloride diuresis. Many studies quantitatively demonstrated the marked natriuretic and chloruretic effect of ethacrynic acid. Some studies showed an average maximal effect in natriuresis resulting in excretion of 17% of the filtered sodium.¹² Initially the predominant anion excreted was chloride, and during the first few days the urinary chloride was equal to the sum of the sodium and potassium cations in the urine. Later, the urinary chloride was less than this sum. The urinary volume increase that accompanied this saluresis was quite variable, ranging from 78% to 808% over mean control rates within 15 minutes in normal individuals following intravenous administration of the drug. The diuretic response diminished with continuous administration but was effectively restored by intermittent administration.

Kaluresis

A definite kaluresis occurred with the use of ethacrynic acid. It was most often seen in normal individuals that were salt depleted as well as in the most avid salt retention patients such as the cirrhotics. The loss of potassium is thought to be an indirect result of ethacrynic acid administration. Due to the direct blockage of sodium and chloride reabsorption, potassium is lost through activation of distal sodium-potassium exchange mechanisms because of the increased amount of sodium diverted to this site. Similar results were obtained whether the drug was given orally or intravenously and differed mainly in time of onset.

The saluretic and diuretic effect was dose related to a certain point, after which larger doses failed to induce a significant difference. Table 1 summarizes the diuretic and saluretic effect of ethacrynic acid in eight normal subjects during eight hours following increasing doses of the drug given orally. Maximum sodium excretion occurred with 150 mgm. orally. The diuretic and natriuretic effects reached their peak at about two hours and lasted from six to eight hours following an oral dose.¹⁰

In addition to the excretion of sodium, chloride, and potassium, ethacrynic acid has additional effects. There is a pattern of increased urinary

TABLE 1*
Mean Results of Urinary Volume and Electrolyte Excretion Over an 8-Hour Period in 8 Normal Subjects after Increasing Single Oral Doses of Ethacrynic Acid

Ethacrynic Acid	Volume (ml.) (Mean $\pm$ S.E.M.)	Sodium (mEq.) (Mean $\pm$ S.E.M.)	Potassium (mEq.) (Mean $\pm$ S.E.M.)	Chloride (mEq.) (Mean $\pm$ S.E.M.)
Control**	408 $\pm$ 36	60 $\pm$ 2	33 $\pm$ 3	64 $\pm$ 2
50 mg.	817 $\pm$ 108	108 $\pm$ 11	43 $\pm$ 5	118 $\pm$ 15
100 mg.	1262 $\pm$ 208	163 $\pm$ 23	52 $\pm$ 7	176 $\pm$ 25
150 mg.	1926 $\pm$ 216	288 $\pm$ 39	62 $\pm$ 7	276 $\pm$ 40
200 mg.	2226 $\pm$ 395	264 $\pm$ 48	67 $\pm$ 8	288 $\pm$ 48
250 mg.	2547 $\pm$ 308	273 $\pm$ 34	75 $\pm$ 8	309 $\pm$ 36

*From Ledingham and Bayliss, Clin Pharmacol Ther 6:476, 1965.

**Mean of three control studies in each of the 8 subjects.

H⁺, NH₄, and titratable acid with a decreased urinary pH and bicarbonate excretion. Again the explanation given is the activation of distally located sodium-hydrogen exchange mechanisms due to the increased sodium load presented at these sites.

Effect on Aldosterone

Ethacrynic acid increased the secretion and excretion of aldosterone in normal individuals.⁷ It has been shown that aldosterone accelerates the distal sodium-potassium exchange mechanism.¹⁷ This increase in aldosterone secondary to ethacrynic acid has been offered as another explanation for kaluresis during its administration. This was substantiated when ethacrynic acid failed to cause a rise in potassium excretion during natruresis and diuresis in an adrenalectomized subject as well as in a patient on aldosterone antagonists.⁸

Effect on Plasma

Changes in certain plasma constituents following oral ethacrynic acid are summarized in Table 2. There was a reduction in plasma volume as judged by the increase in hematocrit and in the concentrations of urea, plasma proteins, and creatinine. There was a decrease in the plasma chloride and potassium concentrations with a reciprocal increase in the bicarbonate concentration. There was essentially no change in the plasma sodium concentration.

Uric Acid

Ethacrynic acid has been shown to have a similar effect on uric acid as seen with the thiazide diuretics.⁷ During oral administration in lower dosages, there is asymptomatic retention and during intravenous administration or much larger oral dosages, there is an increased clearance of uric acid.

Renal Plasma Flow

The effects of ethacrynic acid on the renal plasma flow are variable, and glomerular filtration rate is little effected by the drug. Of interest is the continued effect of the drug in the presence of reduced glomerular filtration rates. In addition, the state of serum chemistries as well as acid-base states seem to have little effect on the effectiveness of this drug.¹³

TABLE 2*
Changes in Certain Plasma Constituents 6 Hours after Single Oral Doses of 100 mg.
and 200 mg. Ethacrynic Acid in a Normal Subject

	Plasma Sodium (mEq/L)	Plasma Potassium (mEq/L)	Plasma Bicarbonate (mEq/L)	Plasma Chloride (mEq/L)	Blood Urea (mg/100 ml.)	Plasma Creatinine (mg/100 ml.)	Hematocrit (Per cent)	Plasma Proteins (Gm/100 ml.)
Before	145	4.8	23	99	35	0.88	45	6.5
6 hours after 100 mg. ethacrynic acid	146	4.3	26	95	42	1.06	48	7.9
Before	145	5.0	23	103	37	0.98	46	6.8
6 hours after 200 mg. ethacrynic acid	146	4.1	27	97	45	1.26	48	7.6

*From Ibid, 6:479, 1965.

Continued

Comparison to Other Diuretics in Magnitude and Mode of Action

Ethacrynic acid has been shown to be functionally as well as structurally different from any other class of diuretic agents.^{4,7,9,11,14,18,19,20}

The Chlorothiazides

When compared to the chlorothiazides, both induce a diuresis of sodium, potassium, and chloride but the site of action is different. As with ethacrynic acid, the free water clearance during water diuresis is decreased, but during hydropenia, there is no decrease in the free water reabsorption when chlorothiazide is used.²¹ This suggests an action distal to the loop of Henle, not involving the counter-current mechanism. The natriuretic potency of ethacrynic acid is four to five times that of the thiazides.⁴ The pattern of excretion of the thiazides is that of decreased urinary H⁺, increased urinary pH, NH₃, and bicarbonate concentration and no change in titratable acid. This pattern is opposite from that obtained with ethacrynic acid. The alkalosis obtained with the thiazides results from potassium loss, not loss of urinary H⁺. The thiazides lower the glomerular filtration rate.

The Mercurials

Ethacrynic acid has been compared to the mercurials in potency but has a different site of action. Both drugs have the same histochemical properties, i.e., the binding of sulfhydryl groups in renal cells. The mercurials act primarily on the proximal tubules as shown by increase in free water clearance and free water reabsorption under appropriate conditions. Ethacrynic acid acts more rapidly but for a shorter and more variable period of time when compared to the mercurials.²⁰ Again, it is the rapidity and the site of action, as well as an opposite pattern of H⁺ excretion, that makes this drug different from the carbonic anhydrase and aldosterone inhibitors. Table 3 compares the acute 48-hour weight loss in pounds, employing the maximal effective dosages of the diuretics in clinical use. Functionally it can be said that the difference in ethacrynic acid from the other classes of diuretics lies in its increased potency, rapidity of onset, variability in length of action, and ability to act under any clinical and acid-base state. The fact that this drug is

TABLE 3*
Acute 48-Hour Weight Loss in Pounds** Comparison
of Various Diuretic Agents

Methyclothiazide	1.9
Chlorthalidone	2.2
Polythiazide	2.5
Trichlormethiazide	2.7
Quinethiazone	2.8
Benzthiazide	3.0
Hydroflumethiazide	3.2
Benzydoflumethiazide	3.3
Cyclothiazide	3.3
Hydrochlorothiazide	3.6
Meralluride	4.5
Ethacrynic Acid	5.8

*From Brest and Others. *Amer J Cardiol* 16:104, 1965.

**Employing maximal effective dosages.

ETHACRYNIC ACID

additive in its action with the other classes of diuretics (especially when used with the carbonic anhydrase inhibitors)⁷ may imply a different mechanism and magnitude of action.

Clinical Application

The Ascites of Cirrhosis

Refractory ascites represents a difficult problem in the management of hepatic cirrhosis. There are many factors that contribute to the accumulation and maintenance of abdominal ascites. These include the renal, adrenal, and cardiovascular factors that play an important role in the retention of salt and water. Shinaberger and Galambos²² list the following adversely modified factors of renal function present in the cirrhotic patient with abdominal ascites.

1. Decreased renal plasma flow.
2. Decreased glomerular filtration rate.
3. Increased proximal tubular reabsorption of sodium and water.
4. Decreased ability to excrete a water load.
5. Increased distal tubular reabsorption of sodium and excretion of potassium under the influence of aldosterone.

Adverse Acid-Base Refractory Ascites

Except for the carbonic anhydrase inhibitors, the other diuretic agents alone or in combination have been effective in therapy. There still remains the group of refractory patients resistant to the usual diuretics. Sherlock and Shaldon²³ and Shinaberger and Galambos²² make the point that the reduced glomerular filtration rate is a major factor in the failure of diuretics in these patients. The development of adverse acid-base states also seems to be a factor contributing to failure. It is on this basis that ethacrynic acid alone or in combination with other diuretics may be

TABLE 4*
Electrolyte Abnormalities Developing During the Course of Diuretic Therapy
with Acid and a Nonchloride Potassium Supplement

Day	Weight	Diuretic Therapy		Clinical State	24-Hour Urine					Serum Electrolytes			
		Etha- cryn- ic Acid	K Supple- ment**		Volume	Creatinine	Na	K	Cl	Na	K	Cl	HCO ₃
	kg.	mg.	meg.		ml.	mg.		mEq.					
0	74.6			Alert	2100	900	2	164		143	5.1		
1	74.6	200	150									100	24
2	73.2	200	150		4700	1175	307	197	446				
3	71.8	200	150										
4	71.3	200	150										
5	68.6	200	150	Encephalo- pathy	3600	1080	140	180	133				
6	68.0	200	150							141	2.8		
7	67.7	200	150		2700	660	140	111	121			86	41
8	67.2	200	150										
9	65.5	200	150		1800	810	31	180					
10	65.7	200	150							143		72	41
11	64.5	200	150										
12	64.7	200	150		3900	980	90		126				
13	62.7	200	150							138	2.7	83	40

*From Lieberman and Reynolds. *Gastroenterology* 49:532, 1965.

**K supplement was given as potassium triplex and effervescent potassium citrate table.

Continued

helpful in the treatment of refractory ascites. Cannon⁷ reported on the use of ethacrynic acid in nine patients with ascites secondary to cirrhosis. All patients were avid sodium retainers, averaging less than 5 mEq. sodium excretion per day. On oral doses of 100 to 200 mgm. per day, the sodium excretion rose from 49 to 437 mEq. per day. Weight loss varied from one-half to 11.5 pounds per day. The electrolyte loss was as reported earlier, and the urinary potassium was higher than in other types of patients treated with the drug.

Four patients were studied on thiazides, mercurials, triamptertine, and spironolactones, and ethacrynic acid was found to be more effective. Lieberman and others²⁴ reported the effects of ethacrynic acid in 32 patients treated over a twelve-month period. All were on a strictly reduced sodium diet. When ethacrynic acid was used with supplemental potassium therapy only, in three patients alkalosis and hypokalemia developed, and two of the three patients went on to a state of hepatic encephalopathy. The dosage of ethacrynic acid was 200 mgm. daily. In eight additional patients in whom a portion of their suggested schedule was used, the effective diuresis occurred as before; but hypokalemic alkalosis developed, and two additional patients developed hepatic encephalopathy. Table 4 illustrates these effects in one of the patients. The authors showed that the alkalosis could occur in the absence of hypokalemia and related the alkalosis to a contraction of the extracellular fluid compartment in the absence of renal loss of bicarbonate.

It can be concluded that the hypochloremic alkalosis and the hypokalemia produced by this potent diuretic may occur as separate electrolyte abnormalities. The authors point out that a simple way of preventing alkalosis is to administer chloride orally in the form of lysine monohydrochloride as a 15% solution. Potassium was supplemented with potassium chloride crystals and the use of spironolactone to decrease the renal loss of potassium. The regimen recommended was as follows²⁴:

1. Lysine monohydrochloride, 25 mEq., q.i.d., on days 1 and 2.
2. Spironolactone (Aldactone-A), 50 mgm., b.i.d., on days 1 and 2.
3. Ethacrynic acid, 100 mgm., b.i.d., on day 3.
4. K Cl, 100 mEq. per day on days 1 and 3, omitted on day 2 to avoid hyperkalemia.

Results

Effective diuresis without significant hypokalemia or alkalosis was obtained in 23 out of 32 patients. Ethacrynic acid should be started at a lower dose and increased to the recommended dose if needed.

Chronic Congestive Heart Failure

The use of ethacrynic acid in patients with fluid retention secondary to chronic congestive heart failure has been reported.^{7,11,20,25} Cannon and others⁷ reported on 14 patients with long-standing congestive heart failure, the majority secondary to arteriosclerotic heart disease. The average sodium loss in the urine for this group of patients was 11 mEq. per day. In the dosage range of 100 to 200 mgm. of ethacrynic acid daily, the rate of excretion rose from 51 to 734 mEq. per day. An effective weight loss was obtained, but all developed hypochloremic alkalosis as treatment continued. There was an associated mild hypokalemia.

A study following two years of experience was reported by Cannon and others.⁸ In a group of 30 patients with chronic congestive heart failure treated over a two-year period, effective mobilization of edema fluid was obtained in 17. The diuretic response diminished with continuous therapy but was effectively restored by intermittent therapy. The better results seem to be in those patients treated for a short period to obtain a rapid mobilization of retained fluid. Daley²⁰ reported on five patients treated with 150 mgm. of ethacrynic acid orally for five days. All patients diuresed, the amount varying with the magnitude of edema present. The diuresis started in one hour, reached a maximum effect in two hours, and maintained a basal level after eight hours. No significant changes in serum electrolytes were reported. Sperber²⁵ reported on 27 patients with congestive heart failure treated over an average period of four months. The authors make the point that the dose must be individualized but that the dosage most often used was 50 mgm. b.i.d. They reported a good response in 80% of the patients. A point that these authors make is that this drug has the ability to reverse a positive sodium balance in the avid sodium retainer when faced with a salt load. Ethacrynic acid provides a measure of protection for the patient who does not adhere to a prescribed low sodium diet.

Acute Pulmonary Edema

In view of its potent diuretic action, the efficacy of long-term use of ethacrynic acid in the cardiac patient remains questionable. However, its properties as a diuretic have encouraged its use in the management of acute pulmonary edema.^{26,27,28} The effect of intravenous ethacrynic acid is seen within minutes and its maximum diuretic activity occurs within 30 minutes. Due to the decrease in cardiac output and resulting reduction in glomerular filtration rate in patients with acute pulmonary edema, other diuretics often give poor results. Fine and Levy²⁸ reported effective results in five patients with acute pulmonary edema given 50 mgm. of ethacrynic acid intravenously along with the usual therapy (not including any other diuretic). The excretion rates of electrolytes were as follows:

Na — 232 microequivalents to 1463 u eq/min.

Cl — 315 microequivalents to 1455 u eq/min.

K — 48 microequivalents to 155 u eq/min.

An average of 600 ml. of urine was lost in a two-hour interval. Rosenberg²⁶ reported good results in 15 patients treated for acute pulmonary edema with 50 mgm. of intravenous ethacrynic acid on admission. The second case summary exemplifies the rapid and potent diuresis with excellent results in the treatment of acute pulmonary edema. Rapid phlebotomy is still the preferred direct approach to a rapidly decreasing venous pooling of blood from the right side of the heart. The use of ethacrynic acid represents a more indirect approach of clearing pulmonary edema by renal excretion of salt and water. In the anemic or hypotensive patient, the rapid diuresis provided by this drug may be essential in the treatment of pulmonary edema. An additional usage of this drug was reported by Ledingham,²⁷ who suggested the prophylactic

Continued

use of 12.5 to 50 mgm. of ethacrynic acid added to each unit of blood prior to transfusion. In the severely anemic patients complicated by fluid retention, the chances of precipitation of pulmonary edema during transfusion are reduced. He reported seven such patients without complication.

Refractory Edema of Renal Disease

The use of ethacrynic acid in the treatment of refractory edema associated with renal disease has also been reported. Hagedorn and others²⁹ noted short-term success in patients with the nephrotic syndrome. Six patients with kidney disease (five out of six biopsy-proven) while on a controlled protein diet, marked sodium restriction, and fluids ad lib., were treated with 100 to 200 mgm. of ethacrynic acid daily. All showed diuresis with weight loss within 24 hours, the maximum decrease in weight and disappearance of edema occurring by the 10th day of therapy. In seven to ten days the sodium and chloride excretion returned to previous control values, and this signaled the completion of the diuretic response. Initially, the potassium excretion increased but not significantly over an extended period of therapy. Maher and Schreiner¹³ treated 30 patients with renal disease. Ethacrynic acid was extremely effective at very low glomerular filtration rates as low as 20 liters/24 hr. and its effect was dose-related. No other diuretic singly or in combination achieved the diuresis equal to that produced by this drug. These authors noted the successful diuresis in a patient with ischemic oliguria with impending tubular necrosis following an episode of hypotension. Mannitol and hydration failed to increase urinary output, while 100 mgm. of ethacrynic acid had good effect. In the patient with circulatory overload the use of a blockade diuretic would be preferred over an osmotically active agent such as Mannitol.

Side Effects

Gastrointestinal Disturbances

A drug as potent as ethacrynic acid has side effects and undesirable results if not carefully monitored during therapy. Gastrointestinal disturbances make up a good part of reported toxic reactions, including nausea, vomiting, and diarrhea.^{2,13,29} Other reactions reported could

TABLE 5*
Possible Toxic Reactions to Ethacrynic Acid:
137 Studies — 38 Patients

Reaction	Patients
Nausea	11
Vomiting	9
Fatigue	4
Dysphagia	3
Apprehension	3
Hypoglycemia	2
Mild hepatic encephalopathy	1
Cholestatic jaundice	1
Rash	1
Pain after injection	1
Acute transient deafness	1
Vertigo	1

*From Maher and Schreiner. *Ann Intern Med* 62:26, 1965.

not be definitely attributed to this drug alone or were inconsistent. Table 5 includes a list of reactions in a study of 38 patients treated with ethacrynic acid.¹³

Electrolyte Acid-Base Disturbances

Undoubtedly the most dangerous toxic effect is the potential electrolyte and acid-base disturbance. The common disorders that develop are a severe hypokalemia and a hypochloremic alkalosis. Hyponatremia does not seem to be a significant problem. Cannon and others³² describe a phenomenon referred to as "contraction" alkalosis following diuresis with ethacrynic acid. This acid-base disturbance results from a significant rapid contraction of the extracellular fluid space following saluresis and diuresis. Since the urinary losses of bicarbonate during diuresis are negligible, the extracellular space contracts around the initial bicarbonate pool. The alkalosis results from this increased bicarbonate concentration.

The situation tends to potentiate itself upon continued usage of the drug due to the continued loss of H⁺ with the returning of additional amounts of new bicarbonate to the extracellular fluid. The kidney is unable to compensate by bicarbonate excretion, for it is stimulated to retain sodium and is presented with a glomerular filtrate relatively poor in chloride. This enhances persistent H⁺ excretion and bicarbonate reabsorption. As was pointed out by Lieberman and Reynolds,²⁴ such a disturbance cannot be corrected unless supplementary chloride as well as potassium is provided during therapy.

Other Disturbances

In the cirrhotic patient the electrolyte disturbance may precipitate *hepatic encephalopathy*.^{7,24} In the cardiac patient who is on digitalis, the loss of potassium, especially over a short period of time as in the treatment of acute pulmonary edema, represents a real danger in developing *digitalis toxicity*. Careful monitoring along with potassium replacement is essential during treatment.

Dixon and others³³ demonstrated the increased ethanol toxicity in mice while on ethacrynic acid. The authors proposed a block by this drug in the formation of acetaldehyde from ethanol and possible serious consequences of alcohol taken during treatment with ethacrynic acid.

Various authors have mentioned *blood dyscrasias* that may be associated with the use of ethacrynic acid.^{2,5,23,34} These include granulocytopenia, thrombocytopenia, and thromboembolic phenomena. Usually the patients were on other drugs that could also be implicated. In our third Case Summary, the patient showed definite bone-marrow depression following the use of ethacrynic acid, but since other drugs were also being used, it is difficult to determine which drug induced depression.

Summary

The management of acute and chronic fluid retention has improved with the development of effective diuretics for both intravenous and oral usage. Ethacrynic acid, a derivative of aryloxyacetic acid, represents a new class of diuretic agents. The drug is transported in the proximal

Continued

portion of the nephron for its direct action within the kidney. It is thought that ethacrynic acid interferes with the sulfhydryl catalyzed enzyme systems within the renal cells. The liver is directly involved in its metabolism and the drug is excreted in the urine and feces. Through renal clearance studies it has been shown that the probable primary site of action within the kidney is the ascending limb of the loop of Henle. Ethacrynic acid causes a direct saluresis of sodium and chloride with a secondary indirect loss of potassium and hydrogen ions. A large concurrent diuresis occurs with the above saluresis. Initial action is seen in minutes following intravenous administration, with a maximal effect in 30 minutes and a duration of action of about two hours. Its potency, rapidity of action, and ability to work under adverse acid-base conditions, as well as its mechanism of action differentiate this drug from other diuretics.

Ethacrynic acid has proven effective when all other diuretics have failed and also has an additive effect when used in conjunction with other diuretics. The dosage of ethacrynic acid must be individualized in clinical usage. Its rapid effect has been especially useful in the treatment of acute pulmonary edema. The most serious side effects result from the electrolyte imbalance following diuresis. The conditions reported are hypokalemia and hypochloremic alkalosis called a contraction alkalosis. This is explained by a reduction in the extracellular fluid space with concomitant renal retention of bicarbonate resulting in an increased bicarbonate concentration. Concurrent administration of potassium and chloride is strongly recommended during ethacrynic acid therapy. Other side effects include gastrointestinal disturbances, asymptomatic uric acid retention, and possible blood dyscrasias.

Case History

Case 1

A 54-year-old white male, with a history of heavy alcohol intake for 30 years, first developed abdominal ascites in February of 1965, at which time he was placed on oral diuretics by his private physician. The patient was referred to Hennepin County General Hospital in November of 1965 and was hospitalized for evaluation of refractory abdominal ascites. On physical examination he had many of the stigmata of Laennec's cirrhosis, including massive abdominal ascites, mild jaundice, wasting of musculature of the shoulder girdle, sparse body hair, spider nevi of the face, neck and chest, and palmar erythema. A liver biopsy confirmed the diagnosis of Laennec's cirrhosis. Attempt at diuresis with mercurials, thiazides, triamterene, and spironolactone was unsuccessful. A regimen using ethacrynic acid as suggested by Lieberman and Reynolds was initiated with excellent results. The patient showed a saluresis with diuresis of 30 pounds over approximately 28 days. He was maintained on a one-gram sodium diet with fluid restriction in the range of 1,000 cc. per day. The patient had no remarkable side effects during treatment. He was discharged and is being followed on the ethacrynic acid regimen in the Outpatient Department.

Case 2

A 51-year-old white male had a history of rheumatic heart disease. There were symptoms in the past suggestive of congestive heart failure, but he was never treated. Five days prior to admission he noted progressive exertional dyspnea with orthopnea and ankle edema. On the night of admission he developed acute respiratory distress and was admitted for treatment of acute pulmonary edema. The patient was critically ill with a blood pressure of 90/0, a pulse of 130 and a respiratory rate of 40. There was marked central and peripheral cyanosis, and central venous pressure measured 34 cm. H₂O. He was given 50 mgm. of ethacrynic acid I. V. along with initial therapy of rotating tourniquets, aminophiline, and digitalization. An immediate diuresis was obtained, and total urine output for the first 24 hours was 4,000 cc.

ETHACRYNIC ACID

The breakdown of urine output during the first 24 hours is shown in the table below. The patient was asymptomatic in 12 hours and had an uneventful hospital course.

	Time	Urine Vol.	Sp. Grav.	
Ethacrynic acid, 50 mgm. I. V.	2:00 a.m.	—	—	Na 133, K 6.2, CO ₂ 14, Cl 89, BUN 28
	4:00 a.m.	2,000	1.005	
	8:00 a.m.	950	1.004	Na 130, K 4.8, CO ₂ 17, Cl 91, BUN 28
	12:00 noon	425	1.008	
	4:00 p.m.	225	1.012	
	8:00 p.m.	250	1.013	
	12:00 a.m.	175	1.018	

Case 3

A 61-year-old woman who was a known alcoholic was admitted with abdominal ascites and bilateral pleural effusions. She was placed on thiazide and triamptere therapy. Since little diuresis occurred, ethacrynic acid was added with good results. Approximately four days after this drug was added, a pancytopenia occurred. A bone marrow was compatible with a toxic depression, probably drug-induced. The patient went on to die due to complications related to her hepatic disease.

References

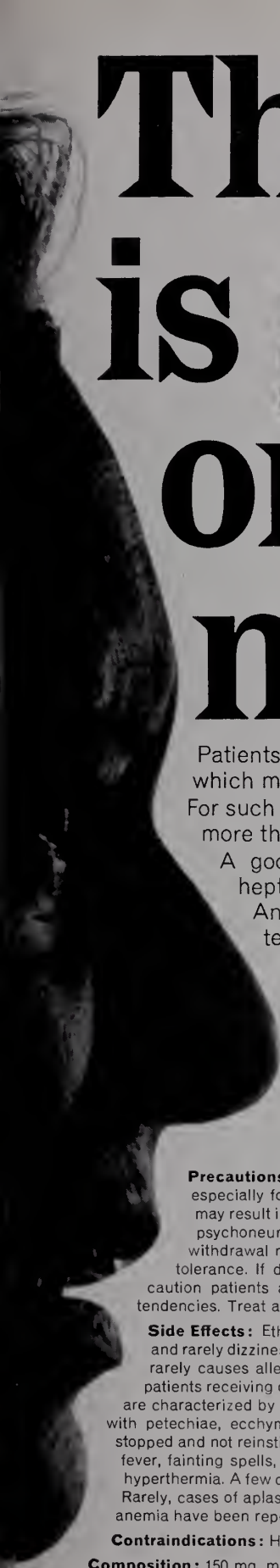
1. Schultz, E. M., Cragoe, E. J., Jr., Becking, J. B., Bolhoffer, W. A., and Sprague, J. M.: *J Med Pharm Chem* 5:660, 1962.
 2. Dollery, C. T.: *The Practitioner* 194:286, 1965.
 3. Goodman, L. S. and Gilman, A.: *The Pharmacological Basis of Therapeutics*, 3rd Edition 847.
 4. Beyer, K. H., Boer, J. E., Michaelson, J. K., and Russo, H. F.: *J Pharmacol Exp Ther* 147:1, 1965.
 5. Sperber, R. J., DeGraff, A. C., and Lyon, A. F.: *Amer Heart J* 69:281, 1965.
 6. Gussin, R. Z. and Cafruny, E. J.: *J Pharmacol Exp Ther* 149:1, 1965.
 7. Cannon, P. J., Ames, R. P., and Laragh, J. H.: *JAMA* 185:854, 1963.
 8. Cannon, P. J., Heinemann, H. O., Stason, W. B., and Laragh, J. H.: *Circulation* 31:5, 1965.
 9. Goldberg, M., McCurdy, D. K., Foltz, E. L., and Bluemle, L. W., Jr.: *J Clin Invest* 43:201, 1964.
 10. Ledingham, J. G. G. and Bayliss, R. T. S.: *Clin Pharmacol Ther* 6:474, 1965.
 11. Bernstein, A., Odze, M., Crews, A., Jr., Rothfeld, E. L. and Simon, F.: *Amer J Med Sci* 249:551, 1965.
- 12-35 May be secured from the Grand Rounds Editor.

MINNESOTA MEDICINE Cover Photographs

In order to encourage more physicians to submit color slides for use on the cover of MINNESOTA MEDICINE the competition is being discontinued. The picture editor now invites all physician-photographers to send 35 mm. color slides of suitable subjects for consideration as cover pictures. The format must be horizontal because of printing limitations. Pictures high-lighting Minnesota seasons, places, and activities will have an automatic advantage. No limit as to the number of slides sent will be set, but all slides should be individually identified. All slides will be returned. Physicians whose pictures are used as covers will be recognized in MINNESOTA MEDICINE. We can use many more pictures than we have received in the past.

Leaders are persons with loud voices, long arms and legs, active elbows, and a determination to stay in front. — Nuggets





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Patients in pain often experience concomitant anxiety and tension, which may add to the burden of pain.

For such patients, you may want to prescribe a preparation that offers more than simple analgesia.

A good choice is often EQUAGESIC® (meprobamate and ethoheptazine citrate with aspirin). It helps relieve pain. And anxiety. And skeletal muscle spasm as related to pain or anxiety and tension.

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Precautions: Keep out of reach of children. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate may result in dependence or habituation in susceptible persons—as ex-addicts, alcoholics, severe psychoneurotics. Withdraw gradually after prolonged high dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance. If drowsiness, ataxia or visual disturbances occur, reduce dose. If symptoms persist, caution patients against operating machinery or driving. Give cautiously to patients with suicidal tendencies. Treat attempted suicide with immediate gastric lavage and appropriate supportive therapy.

Side Effects: Ethoheptazine and aspirin may occasionally cause nausea, vomiting, epigastric distress, and rarely dizziness and CNS depression. Overdosage may result in salicylate intoxication. Meprobamate rarely causes allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. Meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioedema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. A few cases of leukopenia, usually transient, have been reported following prolonged dosage. Rarely, cases of aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported; almost always, in the presence of known toxic agents.

Contraindications: History of sensitivity or severe intolerance to aspirin or meprobamate.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.

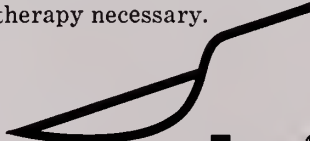
Wyeth Laboratories Philadelphia, Pa.



One by one the family's downed Because the G.I. bug's around

Parepectolin for quick relief of acute diarrhea
... soothes colicky pain with paregoric*
... consolidates fluid stools with pectin
... adsorbs irritants with kaolin,
and protects intestinal mucosa

Whether it's a 24-hour "bug", a food problem,
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will bring the diarrhea under control until etiolo-
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Each fluid ounce of creamy white suspension contains:

*Paregoric (equivalent) (1.0 dram) 3.7 ml.
Contains opium ($\frac{1}{4}$ grain) 15 mg. per fluid
ounce.

warning: may be habit forming

Pectin (2½ grains) 162 mg.
Kaolin (specially purified) . . . (85 grains) 5.5 Gm.
(alcohol 0.69%)

Usual Adult Dose: One or two tablespoonfuls three
times daily.

Usual Children's Dose: One or two teaspoonfuls three
times daily.



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Therapeutic Effects: Tandearil is a nonhormonal compound which may rapidly resolve inflammation and help restore normal joint function. Its action does not affect pituitary-adrenal function or impair immune responses. Its value in osteoarthritis is especially noteworthy because this disorder responds inconsistently to steroids and is often resistant to salicylates. Further, indomethacin is limited only to osteoarthritis of the hip, whereas oxyphenbutazone is effective in all forms of the disease.

Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently.

Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage. Make regular blood counts. Discontinue the drug and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The most common are nausea, edema and drug rash. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, or a generalized allergic reaction may occur and require withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

Dosage in Osteoarthritis: The initial daily dosage in adults is 300-600 mg. in divided daily doses. When improvement occurs, dosage should be decreased to the minimum effective level; this should not exceed 400 mg. daily, and is often achieved with only 100-200 mg. daily.

For complete details, please refer to full prescribing information. 6562-VI(B)R

Availability: Tablets of 100 mg.



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Tandearil®
oxyphenbutazone

helps osteoarthritic
joints move again



3 out of 4 osteoarthritics com-
pletely or markedly improved

Please see ad-
joining page for
brief prescribing
summary

Sperling, I.L.: 3 Years' Experience
with Oxyphenbutazone in the
Treatment of Rheumatic Disorders,
Applied Therapeutics 6:117, 1964.

76.9% of 407 patients

Watts, T.W., Jr.: Treatment of Rheu-
matoid Disorders with Oxyphenbu-
tazone, *Clin. Med.* 73:65, 1966.

84.6% of 39 patients

TA-4919 PC

Life Insurance Settlement Options

In addition to the company from whom you purchase and the type of life insurance contract that you purchase, the method of settlement of the proceeds is of major importance.

Following is a brief summary of the various options available on most policies today. Proper selection of the right combination of options is almost as important as having an adequate amount of insurance.

The Lump-Sum Option: This is self-explanatory. It should be used primarily to provide needed cash immediately, when this cash is not available from other sources.

The Interest Option: The company retains the proceeds and pays a stipulated rate of interest on them. Usually the right to withdraw the proceeds in part, or in total, is vested in the beneficiary. This option is beneficial when income, or cash, is not needed immediately but will be later. This option can be changed to another at a stipulated time or at the beneficiary's discretion.

Income for a Fixed Period: This pays income for a pre-determined fixed period. The amount of income is governed by the period elected and the proceeds available. The most common use for this option is to provide a monthly income for the wife during the dependency period of the children.

Income of a Fixed Amount: This pays income at a certain stipulated rate until the proceeds are exhausted. The number of installments is governed by the proceeds in the company's hands and the stipulated rate of interest. This option is most commonly used where a fixed rate of income is more important than the period for which it is paid.

The Life Income Option: This option provides a stated income to the beneficiary for as long as he, or she, lives. The amount of the income payment for each \$1,000 of proceeds depends upon the number of minimum guaranteed payments (5, 10 or 20 years), the age and the sex of the beneficiary.

Subject to stated minimums, the period of payment under any of these options may be annually, semi-annually, quarterly or monthly.

In addition to these options, the proceeds of an insurance policy may be settled by nearly any combination of options. For example, on a \$12,000 policy, it would be possible to have \$2,000 of the proceeds paid in cash, \$5,000 of the proceeds retained at interest until a stated date, and then paid as a life income with payments guaranteed for five years, \$2,000 paid out in installments for a fixed period of five years, \$1,000 paid out at the rate of \$50 per month until exhausted, and the remaining \$2,000 paid as a life income with payments guaranteed for twenty years. This example illustrates the use of six options on one policy. While such a settlement would be uncommon, it demonstrates the flexibility of planning available through proper use of settlement options.

Settlement options which best fit your individual programs should be utilized. These options are necessarily subject to change with your needs. Your choice of options must be governed by family needs, beneficiaries' ages, and also by your general estate plan provisions. For this reason, your insurance counselor and your attorney should both review your options in order to insure accomplishment of your goals without adversely affecting your estate plan.

William D. Huntington*
Minneapolis, Minnesota

*Northern Division Manager, Professional Management Midwest.

Anatomy Dissection

Until probably sometime during the thirteenth century, the anatomy that was taught to students of medicine was entirely of a theoretical nature, and what was worse, the theories themselves were often quite erroneous. It is believed that the practice of dissection of human bodies for classes in anatomy was started very likely sometime during the thirteenth century. However, it was not until several hundreds of years later that the student did any dissection himself. And even then there were often only two bodies to be dissected in a medical school during a school year. In the early days, the teacher lectured while sitting at his desk as a barber did the dissecting, and a demonstrator pointed out the various structures with a wand. It actually was a couple hundred years before the teacher had acquired enough energy to get off of his fanny and stand beside the cadaver to point out the structures himself.

F. William Saul, M.D.: Pink Pills for Pale People

Prophecy

Don't ever prophesy; for if you prophesy wrong, nobody will forget it; and if you prophesy right, nobody will remember it. — Josh Billings

The owl is therefore the bird of wisdom, because even a fool can see when it is light; it is the wise man that can see when it is dark. — Panin



Abstracts, Briefs and Commentaries

LATE DEVELOPMENT OF PRIMARY CARCINOMA OF THE COLON FOLLOWING URETEROSIGMOIDOSTOMY

This interesting article by members of the departments of Surgery and Pathology of the University of Minnesota is instructive. It represents an extensive review of records and various methods of treatment in a very trying situation. Methods of ureteral diversion date back to 1851 in London. The authors quote Hinman, who in 1936 stated that more than 1,000 techniques had been developed and tried. In 1952 Bricker reported results using ileal segments as substitutes for the urinary bladder. This technique has almost completely replaced the use of ureteral sigmoidostomies for ureteral diversion of urine. However, there are a large number of people still living with modifications of ureterosigmoidostomies.

Seventy-seven bilateral ureteral sigmoidostomies have been performed at the University Hospitals. Ages of patients ranged from four months to 84 years. Of 83 patients, 61 are dead. There were 23 patients who survived 10 years or more; 15 are known to be alive now. Of the 23 patients that survived more than 10 years, two developed proved carcinoma of the colon at the site of the implant. A third patient is reported in great detail. This patient was first admitted in 1945 at age 21, with a 12-year history of chronic interstitial cystitis. She was readmitted in 1948 and bilateral ureterosigmoidostomy was done. She was then readmitted on nine occasions for various complications with hydronephrosis, fever, pain, blood changes, etc. In 1964 a right nephrectomy was performed. In 1965 she developed critical sigmoid obstruction, (17 years after ureterosigmoidostomy) and a double-barrel colostomy was done. She was discharged to return for a sigmoid resection in four weeks. This was done by resection and end-to-end anastomosis.

Pathological study of the removed segment revealed a tumor completely surrounding the ureteral anastomosis. Microscopic sections revealed undifferentiated carcinoma.

Conclusions drawn were that this type of urinary diversion may be associated with an increased risk for development of carcinoma of the colon. Patients having such a procedure should be followed throughout their lives by barium enemas and proctoscopic examinations.

Continued

COMMENT: The authors should be complimented on the excellence of this publication and the care given this patient. The magnitude of this patient's hospital care extending over many years, together with unlimited examinations and operations, would practically preclude the use of a private hospital unless the patient had unlimited insurance coverage. I can highly recommend a review of this original publication for full details.

Stanley R. Maxeiner, Sr., M.D.
Minneapolis, Minnesota

Urdaneta, Luis F., Duffell, David, Crury, C. D., and Aust, J. Bradley: Ann Surg, September, 1966.

MAJOR THORACIC SURGERY AFTER SIXTY

The author reviewed the mortality and morbidity of 340 major thoracic operations in 338 patients ranging in age between 60 and 90 years. The majority of the procedures were for pulmonary lesions. There were no intra-cardiac procedures (7 pacemaker implantations). Of the 338 patients, 186 had some other type of concomitant disease or remote organ involvement by neoplasm. Complicating heart and lung disease became more prominent in the older age group.

Complications were avoided by complementary tracheostomy, empirical preoperative digitalis administration in patients with borderline cardiac reserve, and positive pressure therapy in individuals with pulmonary insufficiency.

There were postoperative complications in 33 patients. Of these, 25 involved the cardiovascular and pulmonary systems. The overall mortality in 338 patients was 3.83% (13 deaths). Interestingly, all deaths occurred in patients below 73 years (19 patients over this age survived without mortality).

COMMENT: This interesting series is heartening. Another report had recorded the postoperative mortality as considerably higher (10-25%) in this same age group with similar lesions.

Jerome T. Grismer, M.D.
Minneapolis, Minnesota

Mauerer: E. R.: Major Thoracic Surgery After Sixty. Ann Thorac Surg 2:806, 1966.

PATENT DUCTUS ARTERIOSUS

The authors of this article review 100 consecutive patients with patent ductus arteriosus treated at the University of Mississippi Medical Center, Jackson, Mississippi. All were treated operatively. There was not a single mortality in the correction of the isolated lesion of patent ductus arteriosus. The authors attribute this brilliant result to successful management of a wide variety of operative and postoperative complications, including hypertensive reaction, pulmonary complications, wound infections, vocal cord paralysis, thoracic duct fistula, and heart failure.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Hardy, James D., Webb, Watts R., Timmis, Hilary, Watson, David G., Blake, Thomas M.: Patent Ductus Arteriosus. Ann Surg 164:5:877, 1966.

THE MYCOPLASMA MYSTERY

In the past, doctors classified nonbacterial pneumonias as "atypical pneumonias." They split the atypical pneumonias into two groups: those without and those with cold agglutinins. The "without" group included those associated with an identifiable cause: ornithosis, Q fever, histoplasmosis. But the "withs" resisted classification and were lumped together under the convenient name "primary atypical pneumonia." Then the lump began to break up.

Virologists scoured the respiratory tree and found a host of possible causes. Among these was an atypical virus called "Eaton Agent." But was "Eaton Agent" a true virus? No, it turned out to be an atypical bacterium — a pleuropneumonia-like organism (PPLO) — in disguise.

In the course of these events the name of the disease was dutifully changed from "primary atypical pneumonia" to "Eaton Agent Pneumonia" to "pleuropneumonia-like pneumonia." The name-calling was not yet over. Bacteriologists had the last word. They pointed out that the PPLO was really a bacterium of the genus mycoplasma. Why not call the disease "Pneumonia due to Mycoplasma Pneumonia?" And so it rests.

Alexander and his co-authors studied the incidence of pneumonia in patients in a large cooperative medical group in Seattle. They observed 1051 cases of pneumonia, an annual rate of 12.9 per 1,000.

The incidence of clinically-recognized pneumonia due to mycoplasma pneumonia was between 1 and 1.5 persons per 1,000. The pneumonia occurred most frequently in children and adolescents and had no seasonal correlation. Patients suffered from headache and fever, but almost none were hospitalized. They complained of upper-respiratory-tract problems more often than in other types of pneumonia, and more often showed white-count elevations. The physicians who saw the patients were usually right when they diagnosed the pneumonias as "atypical" or "viral."

Richard L. Reece, M.D.
Minneapolis, Minnesota

Alexander, R. E., Foy, H. M., Kenny, G. E., Kronmal, R. A., McMahan, R., Clarke, E. R., MacColl, W. A. and Grayston, J. T.: Pneumonia due to Mycoplasma Pneumonia. *New Engl J Med* 275:131, 1966.

MALLORY-WEISS SYNDROME

Review of 20 Cases and Literature Review

Major Holmes reviews 20 cases of Mallory-Weiss syndrome (severe gastrointestinal bleeding from spontaneous mucosal laceration of the esophagus) seen at the Brooke General Hospital in the past 3½ years. This represents 5% of all upper gastrointestinal bleeders seen. Clinical management included emergency esophagoscopy, gastroscopy, and upper gastrointestinal x-rays in all patients with upper gastrointestinal bleeding. Eight patients required surgery in which the mucosal laceration was sutured through a generous gastrotomy incision. The features of Mallory-Weiss syndrome include alcoholic debauch, persistent nausea, vomiting and wrenching followed by massive upper gastrointestinal hemorrhage. These findings were exhibited in the majority of cases reviewed in this article.

Continued

The author suggests that Mallory-Weiss syndrome may be considerably more frequent than current medical literature would indicate and recommended vigorous diagnostic measures in the management of the acute upper gastrointestinal bleeder.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Holmes, Keith D.: Mallory-Weiss Syndrome. Ann Surg 164:5:810, 1966.

LATE RESULTS OF BRONCHIAL RECONSTRUCTION

Rupture of a major bronchus is an uncommon complication of thoracic trauma. Early recognition and treatment, however, are of utmost importance in preserving functioning pulmonary tissue. Current techniques of bronchial repair permit satisfactory anatomical and function reconstruction of injured bronchi. Long-term results have been gratifying.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Ahrari, H., Ekestrom, S. Stockholm, Sweden: Late Results of Bronchial Reconstruction. Ann Surg 164:5:859, 1966.

INTERMITTENT CLAUDICATION

In 198 cases of uncomplicated intermittent claudication followed for five to 12 years or to death, the over-all mortality was 46.5 percent; the mortality at five years was 25 percent. Most of the deaths were due to cardiovascular disease, with myocardial infarction occurring as the commonest lesion.

Age did not affect the prognosis, apart from the fact that older patients have reduced life expectancy in any event. The prognosis was not much affected by the duration of the disease when first seen, whether it was unilateral or bilateral, or the level of the occlusion. Hypertension and pre-existing ischemic heart disease had a harmful effect.

The outlook for the affected limbs was good. In most of the survivors the claudication was either improved or unchanged, but many were disabled by cardiac or cerebral vascular disease. The over-all amputation rate was 7.1 percent and the rate in survivors 6.6 percent. In 69 cases a lumbar sympathectomy was done, chiefly for ischemic changes in the feet. Some benefited from the operation.

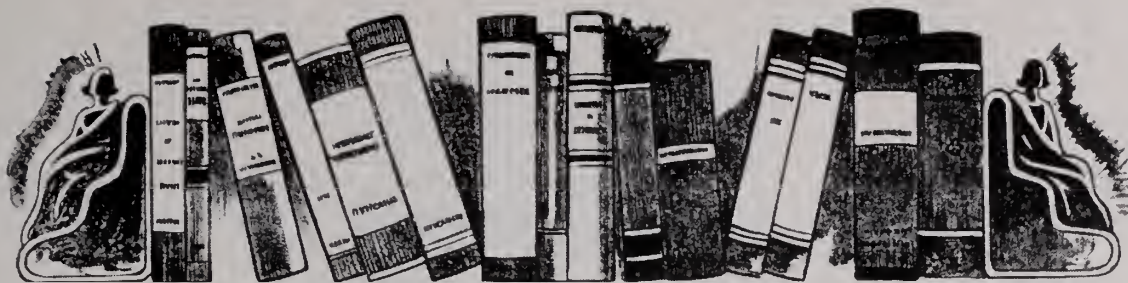
Claudication indicates atherosclerosis, usually generalized; this fact is emphasized when the ten-year survival rate is compared with that of patients who had angina or survived a myocardial infarction, for the results are similar. Treatment, whether medical or surgical, should be assessed in the light of these observations.

Courtesy of World-Wide Abstracts

Begg, T., and Richards, R.: Scottish Med J 7/8:341.

Take Your Choice

At each minute we are obliterated by the idea and the sensation of time. And there are only two ways of escape from this nightmare, of forgetting it: pleasure and work. Pleasure anuses us. Work fortifies us. Let us choose. — Baudelaire



Book Reviews

The whole object of education is, or should be, to develop mind. The mind should be a thing that works. It should be able to pass judgment on events as they arise, make decisions. — Sherwood Anderson

**DIE ARTHROSIS DEFORMANS DES KNEIGEL-
ENKES** — Walter Mohing, Springer-Verlag Berlin
Heidelberg New York 1966.

The need of a uniform classification of joint disease becomes immediately apparent when one takes up the first task of simply translating the title of this book. Literally it is "The Deforming Arthrosis of The Knee Joints." The term arthrosis is not used much in the English literature and most would be inclined to translate this as degenerative arthritis or osteoarthritis of the knee. Nevertheless this is an excellent 212-page treatise dealing with degenerative arthritis of the knee from the point of view of the influence of static-mechanical factors in the cause, progression, and localization of knee joint changes. The author is an orthopedist and he bases his text on a personal experience of 2000 cases.

There is an introductory chapter on anatomy and the mechanics of knee joint motion. The major portion of the text deals in considerable detail with individual entities that have caused a secondary arthritis, such as congenital disorders, post-traumatic disorders, obesity, and patellar pathology. There are numerous and excellent photographs and x-rays throughout. The chapter on treatment is brief but to the point. There is an extensive bibliography referring primarily to the German literature which includes the year 1963. The book will be primarily of interest to orthopedists, rheumatologists, and physiatrists, although other physicians with a knowledge of German should be able to gather some useful information from the text.

Paul J. Bilka, M.D.
Minneapolis, Minn.

PATHOLOGY — 5th Edition, 2 Volumes, edited by
W. A. D. Anderson, 1,439 pages, 1,267 illustrations.
C. V. Mosby Company, St. Louis, Missouri, 1966.
\$21.00.

PATHOLOGY made its debut in 1948. Because of the skills of its knowledge broker, editor W. A. D. Anderson, it quickly became the premier bluechip textbook of pathology. He carefully picked his contributors, diligently compressed their prose and kept his eye on the fact market. As information expanded, the book grew. By its fourth edition in

1961, it weighed an unwieldy nine pounds. Anderson, always alert to the needs of his readers, has solved the problem by carrying out a 2:1 split.

The two volumes making up the fifth edition are organized similarly to its single-volume predecessor. Thirty-nine contributors present a systematic, comprehensive, and balanced organ system review. The descriptions are condensed, the photomicrographs clear, and the references apt. According to the preface, the purpose of the book is to satisfy the whims of beginners, pedagogues and practitioners. This is an impossible task. Such a trio will find nits to pick in any book, especially a fundamental text that attempts to blanket a sprawling field. But I think Anderson has come close to his goal. In my opinion, the divided *Anderson* still stands several notches above its competitors.

Richard L. Reece, M.D.
Minneapolis, Minnesota

MODERN TREATMENT — Treatment of Gastro-
intestinal Infections; Treatment of Superinfections.
Edited by Marcel Patterson and Harold J. Simon.
Harper and Row, New York, 1966.

MODERN TREATMENT is published as a bimonthly paperback volume, each number considering one or two fields of medicine. Patterson, editing the gastrointestinal portion, notes that these infections have become uncommon in this country because of painstaking work in the food industry and public health.

However, the occasional breakdown in sanitation still poses a considerable threat of intestinal disease. The increasing urbanization of population means that sanitation failures can result in massive epidemics.

Advances have been in control rather than therapy of disease. Potential for serious gastrointestinal infection is constant. In this day of instant travel with the entire earth no more than twelve hours away from any airport, we can no longer comfortably assume that exotic diseases, particularly gastrointestinal infestations, will not present themselves locally.

The discussion edited by Simon concerns opportunistic infections. These are the ever menacing factors that complicate all phases of surgery.

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A man will sometimes devote all his life to the development of one part of his body — the wishbone. — Frost

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Religion in American Life

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Special Article

Blood Group Antibodies in Prenatal Sera

Results
of
Screening
43,000
Individuals*

HERBERT F. POLESKY, M.D.**
Minneapolis, Minnesota

SINCE LEVINE and Stetson's original observation in 1939¹ of the role of isoimmunization in the etiology of erythroblastosis fetalis, it has become almost universal practice to test for anti-Rh^o (D) antibodies in the sera of Rh negative, pregnant women. During the same period of time, the number of established blood groups has expanded from three to fifteen. There are now well over 100 documented blood group antigens, making it possible to recognize over a million individual combinations of blood group factors. Many of these antigens have been found as the result of maternal sensitization, hemolytic disease of the newborn, and transfusion reactions. In the last six years, sera from 43,000 pregnant individuals have been studied on one or more occasions for atypical blood group antibodies, at the Minneapolis War Memorial Blood Bank. It is the purpose of this paper to report the results of this screening program and to discuss the significance of the antibodies found.

Materials and Methods

Five to 10 cc. samples of clotted blood were received by mail.

Erythrocytes were typed with anti-A, anti-B, anti-A,B (O serum), anti-Rh^o(D), anti-rh'(C), anti-rh''(E), anti-hr'(c), and anti-hr''(e). The patients' sera were checked with known type A₁, B, and O erythrocytes. Each serum was screened for antibodies with a pool of red cells from three selected donors. These cells contain the majority of antigens likely to occur in the population being tested. The same donors were drawn every two weeks and their cells stored in ACD solution without preservatives. The screening procedure used was as follows:

1. Incubation of 2-4% saline suspension of selected donor cells with 0.1 cc. of patient serum at 16 to 20°C. for one hour.† Continued

*Presented in part at the Minnesota Association of Blood Banks meeting, May 4, 1966, Minneapolis, Minnesota.

**Assistant Professor, Department of Laboratory Medicine, University of Minnesota and Director of the Minneapolis War Memorial Blood Bank.

†Sample centrifuged and observed for agglutination and hemolysis.

2. Incubation of the same suspension at 37°C. for one hour.*

3. Previous incubation mixture washed three times and antihuman globulin added.*

4. Incubation of 2-4% suspension of washed, papainized, pooled cells with 0.1 cc. of patient's serum at 37°C. for 30 minutes.*

5. Incubation of 2-4% suspension of selected pooled cells with one drop of 30% albumin and one drop of patient's serum at 16-20° for 10 minutes.*

Identification of the antibody or antibodies in all sera with a positive screening test was carried out with a panel of erythrocytes of known antigenic composition. The same donors used in the screening pools form part of the panel which was supplemented by frozen cells to aid in the identification of

*Sample centrifuged and observed for agglutination and hemolysis.

TABLE 1
Antibodies To Rh Antigens

	Number Of Individuals With Antibodies		
	Rh ^o Positive	Rh ^o Negative	Total
Anti-Rh ^o (D)	—	1412	1412
Anti-rh'(C)	2	3	5
Anti-rh'' ^w (C ^w)	4	—	4
Anti-rh''(E)	44	10	54
Anti-hr'(c)	51	—	51
Anti-hr''(e)	2	—	2
Anti-Rh ^o + rh'(CD)	—	443	443
Anti-Rh ^o + rh''(DE)	—	9	9
Anti-hr' + rh''(cE)	17	—	17
Multiple Antibodies	(16)*	27	27
	120	1904	2024

*Included in above categories.

multiple and/or rare antibodies. Additional typing of the patient's cells and her husband's cells was performed as indicated.

Results

Of the women tested 35.2% typed as Rh negative. Of these individuals 13.9% had positive antibody screening tests. Of the Rh positive women 1.3% were found to have antibodies. Of the individuals with antibodies 82% showed specificity for antigens in the Rh system. In Table 1, the distribution of these is shown in the two groups of patients. Of the women with Rh antibodies 25% reacted positively with more than one Rh and/or other blood group factor. In Table 2, a similar comparison between the Rh negative and the Rh positive women is shown for antibodies to red cell antigens in other blood group systems. The high incidence of Lewis and Kell antibodies observed in this study is similar to the observations of Kissmeyer-Nielsen,² Bowman,³ and Giblett.⁴

Discussion

The results of this study corroborate the findings of Bowman³ that atypical blood group antibodies occur in 4% of appropriately studied prenatal sera. The higher incidence observed by us (Table 3) can be accounted for by the pre-selection of the specimens submitted for study, since our data was obtained from a group of women with more than double the expected distribution of Rh negatives. In Table 3 the 5.7% incidence of antibodies detected in our laboratory is compared with the findings reported from other centers using similar procedures.

TABLE 2
Antibodies to Other Blood Group Antigens

Blood Group System	Number of Individuals with Antibodies			Specificity of Antibodies
	Rh ^o Positive	Rh ^o Negative	Total	
Lewis	46	48	94	Le ^a 68, Le ^b , 15, Le ^a + Le ^b 11
Kell	57	36	93	K 91, Kp ^a 1, Kp ^b 1
ABH	41	39	80	OH 66, A ₁ 14
MNSs	24	21	45	M 32, N 3, S 10
P	11	16	27	P ₁ 27
Duffy	12	5	17	Fy ^a 16, Fy ^b 1
I i	10	3	13	I 13
Kidd	2	5	7	Jk ^a 7
Other	31	29	60	Non-specific cold 46, Unidentified 9, Lu ^b 1, Yt ^a 1, Wt ^a 1, Gy ^a 2
Total	234	202	436	

BLOOD GROUP ANTIBODIES

TABLE 3
Incidence of Positive Antibody Screening Tests

	No. of Patients	Antibodies	%
Rh Laboratory, MWMBB	43,000	2460	5.7
Donors, MWMBB	185,000	373	0.2
Recipients (E. Giblett) ⁴	21,000		1.3
Prenatal Sera (H. S. Bowman) ³	4,653	179	3.9
Random (F. Kissmeyer-Nielsen) ²	200,000	4168	2.1

Kissmeyer-Nielsen² found that 1/590 Rh positive individuals had antibodies. The sera he studied included donors, recipients, compatibility problems, and prenatal patients; thus his study is fairly representative of the population at large. Our data indicates that 1/77 Rh positive pregnant women is sensitized. When compared to the general population, both Rh positive and Rh negative pregnant women are highly likely to have been sensitized. In spite of the increased risk to all gravid women, the skewed distribution of the Rh type of the samples submitted for study (35% Rh negative) confirms our impression that once a woman is classified as Rh positive, it is unlikely that she will be screened for antibodies during pregnancy.

Two major categories of problems can be anticipated from the finding of atypical antibodies in prenatal sera: (1) compatibility testing may be difficult and the risk of a transfusion reaction increased, and (2) hemolytic disease of the newborn may be present. A large number of antibodies frequently encountered during pregnancy either do not cross the placenta or have a specificity to antigens weakly developed or absent in the neonate. This group which has not been reported to cause erythroblastosis, but which can cause transfusion reactions, includes anti-Le^a, anti-Le^b, anti-A₁, anti-I, anti-OH, anti-P₁, anti-N, anti-Yt^a, and Gy^a.⁵ The remainder of the antibodies detected, all potentially capable of causing severe transfusion reactions, have been reported to cause hemolytic disease of the newborn.

A more detailed examination of the data obtained on women with anti-Kell points out the importance of typing the patient's husband and the value of a history in clarifying

the possible problems that may be encountered. In Table 4 it can be seen that only 14 of 59 patients whose husbands were typed for Kell were married to Kell positive men. A history of transfusion was obtained from almost half of those individuals married to Kell negatives. Since the histories were incomplete, it is highly probable that all of these women had received transfusions at one time. Thus in those cases where the husband is kk, both the physician and patient can be reassured that the baby will not be affected by erythroblastosis and the transfusion service warned of a potential recipient sensitized to Kell. Similar situations can occur with other blood group antigens, and it is not unusual to find a woman sensitized by prior transfusion or pregnancy during a previous marriage.

TABLE 4

Antibodies to Kell	% Known to Have Been Transfused	
Number of Women with anti-K	91	31
Husband — Kell type Known	59	
Husband Kell Positive	14	14
Husband Kell Negative (kk)	45	44

Summary

Atypical blood group antibodies were found in the sera of 5.7% of 43,000 pregnant women. Of these 14.4% were in Rh positive individuals.

The finding of antibodies in prenatal serum is useful in predicting the possibility of erythroblastosis and crossmatch problems. Since the yield of such a screening program is high and can contribute to the safety of the patient, sera from all pregnant women regardless of Rh type should be tested.

References

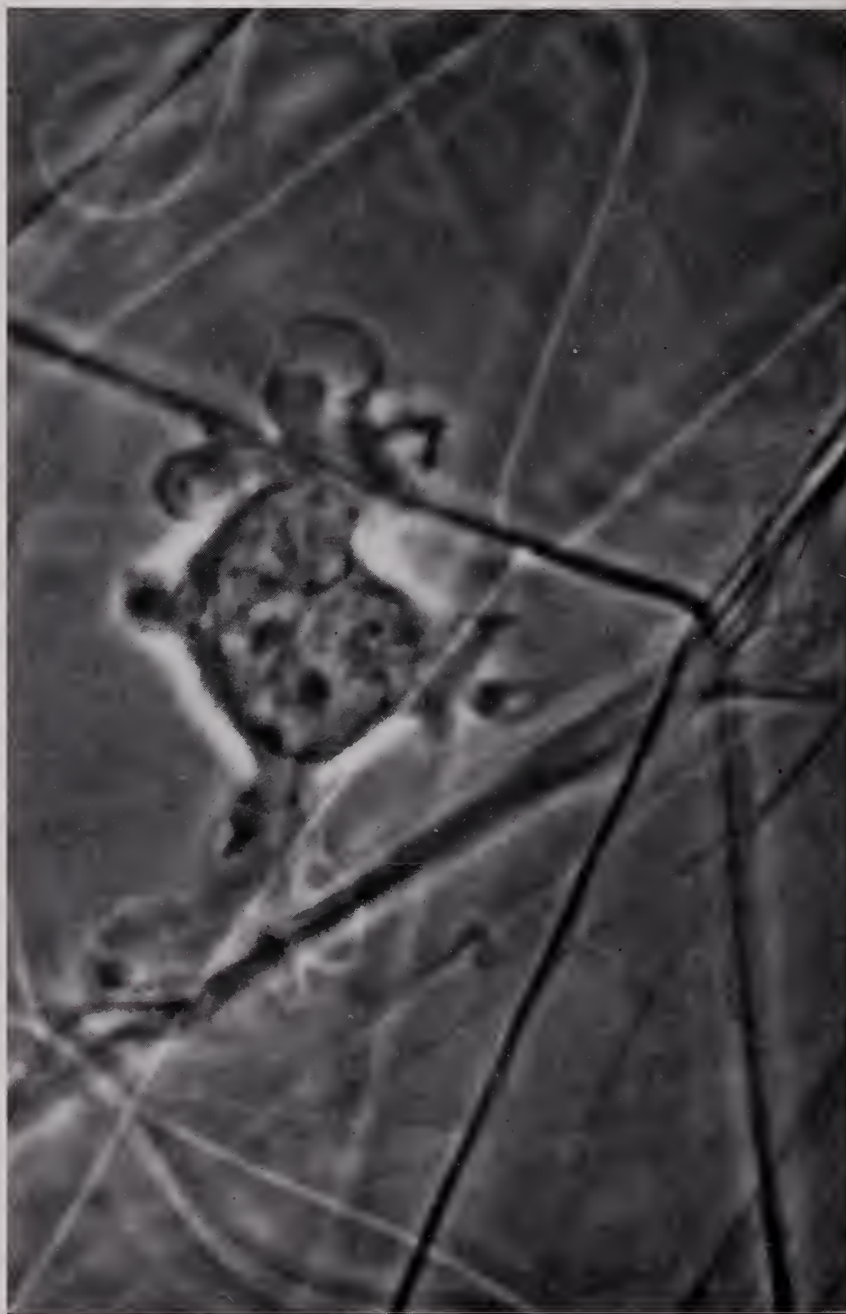
1. Levine, P. and Stetson, R. E.: An Unusual Case of Intragroup Agglutination. *JAMA* 113:126, 1939.
- 2-5 May be secured from the author or the reprints.

INFLAMMATION: A cellular fight for life

A SYNTEX REPORT based on recently developed hypotheses about topical corticosteroids, including the cellular theories of inflammation by Thomas F. Dougherty, Ph.D., University of Utah.

You are looking at a fibroblast fighting for life. This cell—one of the most common found in connective tissue—has literally been poisoned by cytotoxins released from other cells that have ruptured. Soon, if the abnormal activity of this fibroblast does not cease, it, too, will rupture and die—one more casualty in the inflammatory wave of destruction precipitated by injury.

Until a short time ago no one had ever witnessed such a scene at the cellular level. Now, through advanced cinemicrographic techniques, it is possible to view and photograph the inflammatory process as produced experimentally in living animal tissue. This method permits new insight into the mechanism of inflammation and the role of corticosteroids in therapeutic management. Equally important, these techniques shed new light on factors that may make one corticosteroid more effective than another—factors that can be correlated with other chemical, biologic, and clinical parameters.

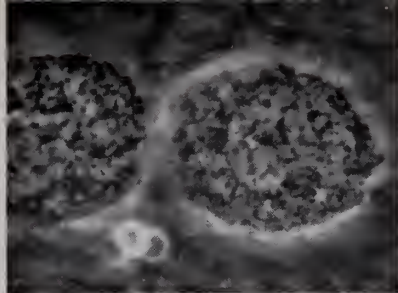


Visual evidence of how corticosteroids influence the inflammatory reaction

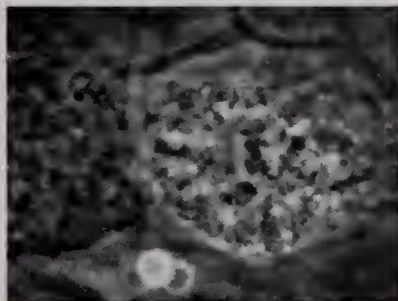
Working with phase-contrast cine-micrography on living animal tissue, Doctors Thomas F. Dougherty and David Berliner of the University of Utah College of Medicine have actually filmed cellular events that occur during the inflammatory reaction. This remarkable study* and additional work by these investigators, as well as by others, have established a new theoretical biologic basis for the antiinflammatory effect of the corticosteroids. (It must be noted that other theories, such as the lysosome or so-called "suicide bag" theory, have been postulated, although it is quite likely that there are more similarities than differences among the various theoretical models.)

The inflammatory wave of destruction

In this investigation an injurious injection of gelatin is used to set off an inflammatory reaction in living mouse tissue. What follows is a wave of destructive cellular activity that comprises the inflammatory response to injury. Mast cells (which contain heparin, serotonin and histamine) take up water, swell and rupture, releasing their contents, which are toxic outside the mast cell wall. These toxins, in turn, cause disintegration of other cells (such as fibroblasts) and the release of additional toxic material. Capillaries, too, take up water and leak unformed blood elements, causing edema. And polymorphonuclears, lymphocytes and perithelial cells invade the inflamed site. As a result of all these changes, the cellular environment reaches a state of turmoil.



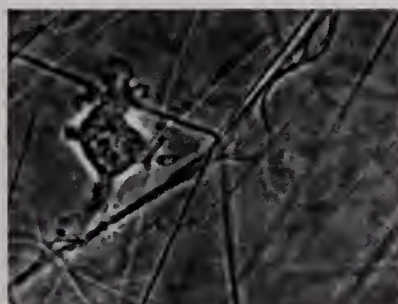
Phase-contrast microscopy showing mast cell before injury.



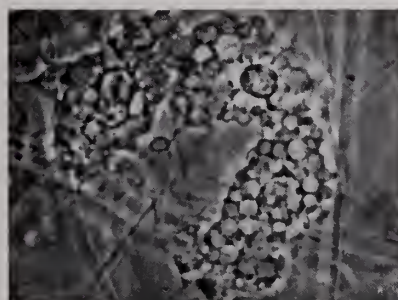
Mast cell (after injury) has broken up and released cytotoxins.

How corticosteroids change the picture

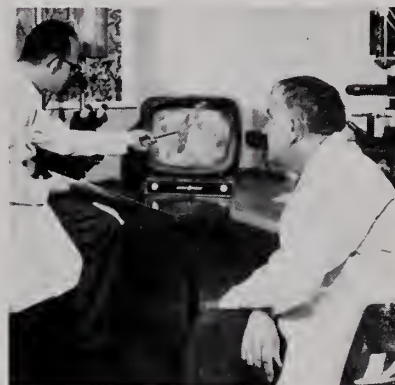
Corticosteroids appear to virtually stop the abnormal cellular activity that constitutes the inflammatory reaction. This permits the body's natural resources to clear up the inflamed area and repair the damaged tissue. This interpretation is supported by the fact that when the injurious gelatin solution is injected simultaneously with a corticosteroid — Synalar (fluocinolone acetonide) — the inflammatory pattern simply does not develop.



Fibroblast in high state of activity, much distorted.



Mast cells showing effects of corticosteroid action: cells are normal in size, shape and activity.

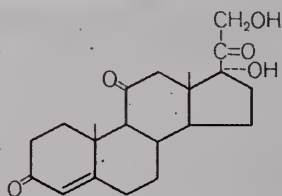


In summarizing his study Doctor Dougherty states: "...we also feel this work may explain why one corticosteroid helps a patient more rapidly and effectively than another. If it does, it is because one corticosteroid is the fastest, most effective inhibitor of the series of inflammatory events at the tissue level."

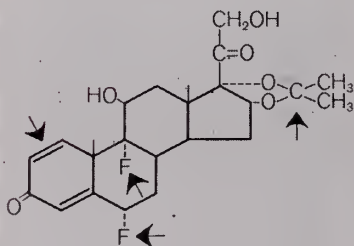
*A New View of Corticosteroid Action in Inflammatory Dermatoses, a film based on this study, is now available from your Syntex representative.

How advances in chemical design have achieved greater steroid potency

The chemical modification of corticosteroid molecules from the advent of hydrocortisone to the development of Synalar (fluocinolone acetonide) is a prime example of how biochemists can "design" to increase therapeutic activity and minimize undesirable side actions. Below, for example, we see the important changes that were made in reference to the hydrocortisone molecule to produce fluocinolone acetonide, one of the most active of all topical corticosteroids. As a result, a 0.01% preparation of Synalar (fluocinolone acetonide) has been reported to do the work of a 1% hydrocortisone product containing 100 times more corticosteroid. And it can often do it more effectively.



Hydrocortisone

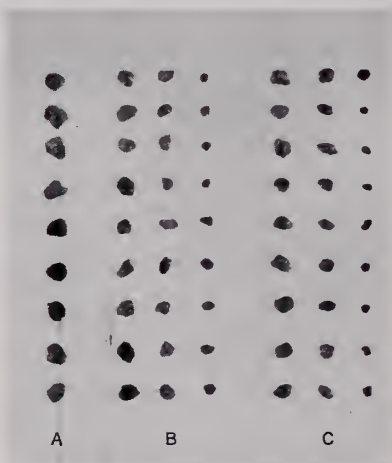


Fluocinolone Acetonide (Synalar)

- a double bond between carbons 1 and 2
- fluorine substitutions at both the 6- α , and the 9- α positions
- the addition of the acetonide at the 16- α , 17- α positions, thus providing one of the most potent topical corticosteroids available.

How bioassay tests are used to "predict" therapeutic potential

Biologic assays are another tool used by researchers to help establish the relative activity of corticosteroids. To date no single method of assaying corticosteroid activity has emerged as the ideal "yardstick" for predicting therapeutic potential. Taken together, however, these methods have proved useful. When such tests are run on various corticosteroids, a definite order of corticosteroid activity becomes evident. Compounds with the highest order of activity may be expected to merit clinical trial to establish their high therapeutic potential. When assayed by these methods, fluocinolone acetonide (Synalar) emerges as one of the most active topical corticosteroids, milligram for milligram, available for clinical application today.



THE THYMUS INVOLUTION ASSAY¹⁻⁴ is run on adrenalectomized rats. The sizes of the glands are measured, and the degree of involution caused by the steroid is determined as an indication of its potency. In the above photo, the comparative involution of thymus glands achieved with hydrocortisone and Synalar (fluocinolone acetonide) is shown. Untreated controls (A) show normal size. Group B— injected with 1, 2 and 4 mg. of hydrocortisone— show progressively smaller thymuses as does Group C— injected with fluocinolone acetonide— but with only 1/500th the dose of hydrocortisone.



THE ANTIGRANULOMA ASSAY¹⁻⁴ also utilizes adrenalectomized rats. Granulomas are induced by subcutaneous implantation of cotton pellets on either side of the thorax. The degree of granuloma inhibition achieved by a steroid reflects its potency. The above photo shows the inhibition of granuloma formation achieved with hydrocortisone and Synalar (fluocinolone acetonide). Untreated controls (A) show large, red granulomas adhering to the pellets. Group B, receiving hydrocortisone and Group C, receiving fluocinolone acetonide, show little, if any, granuloma formation. Fluocinolone acetonide produced the same effect as hydrocortisone with only 1/500th the dose. This assay, as well as the thymus involution assay, measures systemic rather than topical corticosteroid activity. Nevertheless, results by these methods correlate well with other assays and with the milligram potencies of topical steroids in current clinical use.

Worldwide clinical experience confirms the predictable therapeutic potential of Synalar

It is particularly gratifying that the promise of the advanced chemical design and high order of bioassay activity of Synalar (fluocinolone acetonide) has been confirmed by widespread therapeutic application. Indeed, the impressive clinical response rate of Synalar has been documented in no fewer than 232 papers from 22 countries.

PRESCRIBING INFORMATION

For initiation of therapy: Cream 0.025%, 5 and 15 Gm. tubes, 425 Gm. jars; *for emollient effect:* Ointment 0.025%, 15 Gm. tubes; *for maintenance therapy:* Cream 0.01%, 15 and 45 Gm. tubes, 120 Gm. jars; *for intertriginous or hairy sites:* Solution 0.01%, 20 cc. and 60 cc. plastic squeeze bottles; *for infected inflammatory dermatoses:* Neo-Synalar® Cream (0.025% fluocinolone acetonide, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes.

CONTRAINDICATIONS: Tuberculous, fungal, and most viral lesions of the skin, (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. **PRECAUTIONS:** Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for pro-

Representative Clinical Results with Synalar*

Efficacy Documented in over 4,000 Patients

Condition	Number of Publications	Number of Patients	Significant Improvement†
Contact Dermatitis	27	750	713
Eczematous Dermatitis	21	472	409
Seborrheic Dermatitis	18	442	426
Atopic Dermatitis	24	460	426
Psoriasis	36	1,699	1,510
Neurodermatitis	18	351	324
Total	144	4,174	3,808

*Complete bibliography on request.

†Expressed by the authors as excellent, very good, good, complete remission of inflammation, etc.

longed periods of time. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. When severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. **SIDE EFFECTS:** Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. The neomycin in Neo-Synalar Cream rarely produces allergic reactions.

REFERENCES: 1. Lerner, L. J., Bianchi, A., Turkheimer, A. R., Singer, F. M., and Borman, A.: Anti-inflammatory steroids: potency, duration and modification of activities. *Ann NY Acad Sci* 116:1071 (Aug. 27) 1964. 2. Idem: Comparison of anti-granuloma, thymolytic and glucocorticoid activities of anti-inflammatory steroids. *Proc Soc Exp Biol Med* 116:385 (June) 1964. 3. Ringler, A.: Activities of adrenocorticosteroids in experimental animals and man, in Dorfman, R. I.: *Methods of hormone research*, New York, Academic Press, 1964, vol. III, pp. 234-280. 4. Gubersky, V. R.: To be published.

fluocinolone acetonide — an original steroid from
SYNTEX
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For inflammatory
dermatoses...
by any measure
a topical corticosteroid
of choice

Synalar® (fluocinolone acetonide)

Milligram for milligram
one of the most active topical
corticosteroids available

Rapid and predictable
in antiinflammatory and
antipruritic activity

Results often comparable to
those of systemic corticosteroids
with fewer hazards

114th Annual Meeting

Duluth Will Host Our Annual Meeting



Mark your calendar . . .

The committee on scientific assembly has made a number of significant innovations in the format of our 1967 Annual Meeting May 15, 16 and 17 in Duluth.

For the first time we will meet in the exciting environment of the new \$6.1 million Duluth Civic Auditorium. The spacious new facility will house most of the meeting events, including the House of Delegates meetings, scientific sessions, scientific and technical exhibits, and the round table luncheons; also most breakfast meetings.

A home study course on erythroblastosis fetalis has been arranged by the committee to enable physicians to continue their education, to participate in the scientific session with greater depth, and to better serve their patients. Approximately 100 physicians have enrolled for the course, offered during the six weeks preceding the seminar on this subject, to be held Tuesday, May 16.

The presentation of a series of eleven five minute "How To Do It" talks to be given by Minnesota physicians will be one of the new features of the 1967 scientific assembly program. Topics scheduled for discussion at this session, set for 3:30 P.M. Monday, May 15, include: Warts Cooking?; Constipation — Can't or Won't?; The Plugged Catheter; Bloody Nose; Threatened Abortion; Painful Feet; Contact Lenses; The Buzzing Ear; The Discharging Nipple; How to Inject a Painful Shoulder; and The Varicose Ulcer.

A timely discussion entitled "The Intensive Care Unit — Can the Community Hospital Afford It?" will be featured at the 10:30 A.M. session Monday, May 15.

Medicine and Religion, a perennially popular subject among those attending annual meetings, will be featured at the 2:00 P.M. session Monday, May 15. "M.D., L.L.B., and D.D. — Whither Goest Thou?" is the title selected by the committee, and thorny philosophical and legal problems connected with transplants and other dramatic modern developments will be considered.

Other scientific sessions scheduled will be

devoted to dangerous drug problems, "Convulsive Disorders, Fertility and Sterility" and medical emergencies under the title, "Doctor Blue — Where Are You?"

Two groups of round table luncheons will be held, Monday and Tuesday noon. Monday round table luncheon subjects are: The Hearing Aid Problem, Dialysis in the Community Hospital and the Home, Cancer Chemotherapy, Ongoing Coronary Disease, Field Diagnosis in Athletic Injuries, The Annual Physical — Why? and The Neuter Sex.

Six luncheons have been scheduled for Tuesday noon. Luncheon topics are: Drug Incompatibilities, Erythroblastosis, Diagnosis of the Unconscious Patient, The Thrombosed Hemorrhoid, Multiple Pregnancy, and Medical and Surgical Treatment of Persistent Peptic Ulcers. Distinguished guest speakers will join local authorities as leaders for both days luncheons.

The House of Delegates will convene Sunday, May 14, at 2:00 P.M. and Tuesday, May 16, at 10:00 A.M. Our Annual Banquet, including the reception, presentations, entertainment, dancing and late evening entertainment, is set for Tuesday evening, May 16.

The Wednesday program will be devoted to current socio-economic problems.

As in the past, many scientific and non-scientific committees have planned breakfast meetings in conjunction with the scientific sessions. Also, a particularly outstanding selection of scientific and technical exhibitors has accepted the invitation to exhibit with us in the new Duluth Auditorium.

The committee extends a special invitation to all physicians to visit the exhibits, and urges them to express their appreciation to the technical exhibitors whose participation annually helps to make this meeting possible.

A complete listing of all the details of the scientific, social and business sessions will be included in the official program which will be mailed to all physicians. Consult the Annual Meeting program for complete details. Following is an abbreviated schedule of scientific events and speakers.

Scientific Program

Duluth Civic Auditorium

MONDAY MORNING, MAY 15, 1967

The program on Monday is acceptable for 4½ accredited hours by the American Academy of General Practice.

A.M. Visit scientific and technical exhibits

9:00 Doctor Blue — Where Are You?

Cardiopulmonary Emergencies in Infants — *Harold Katkov, Wayzata*

Complete Heart Block and Associated Ventricular Arrhythmias — *Stephen M. Ayres, New York*

Cardiac Resuscitation — *Carlos E. Harrison, Jr., Rochester*

10:30 Visit scientific and technical exhibits

10:30 THE INTENSIVE CARE UNIT — CAN THE COMMUNITY HOSPITAL AFFORD IT?

Wilbert S. Henke, St. Paul

Richard C. Gaard, Robbinsdale

Mr. Jerre Logan, St. Paul

Mr. Jerome T. Bieter, Hamilton Associates, Minneapolis

MONDAY AFTERNOON

P.M.

12:15 ROUND TABLE LUNCHEONS

1:30 Visit scientific and technical exhibits

2:00 M.D., L.L.B., AND D.D. — WHITHER GOEST THOU?

Eugene E. Scott, St. Paul — Moderator

Rev. Paul B. McCleave, Chicago

Thomas E. Starzl, Denver

Mr. Burr B. Markham, Minneapolis

3:00 Visit scientific and technical exhibits

3:30 HOW TO DO IT (Five minute talks)

1. Warts Cooking?

E. T. Ceder, Minneapolis

2. Constipation — Can't or Won't?

Felix A. McParland, Jr., Minneapolis

3. The Plugged Catheter

4. Bloody Nose

O. E. Hallberg, Rochester

5. Threatened Abortion

Carl E. Johnson, Rochester

6. Painful Feet

Kenath H. Sponsel, Minneapolis

7. Contact Lenses

Theodore R. Fritzsche, New Ulm

8. The Buzzing Ear

Barelay M. Cram, St. Paul

9. The Discharging Nipple

David P. Anderson, Jr., Austin

10. How To Inject a Painful Shoulder

Charles G. Sheppard, St. Peter

11. The Varicose Ulcer

Erie P. Lofgren, Rochester

TUESDAY MORNING, MAY 16, 1967

The program on Tuesday is acceptable for 4½ accredited hours by the American Academy of General Practice.

A.M. Visit scientific and technical exhibits

9:00 IATROGENIC MEDICAL PROBLEMS — DANGEROUS DRUGS

Raymond N. Bieter, Minneapolis

Edward A. Carr, Jr., Ann Arbor, Michigan

10:00 Visit scientific and technical exhibits

10:30 ERYTHROBLASTOSIS

Peter J. Bartzén, Duluth — moderator

John M. Bowman, Winnipeg

R. F. Friesen, Winnipeg

J. E. Wall, Duluth

Donald Larson, Duluth

TUESDAY AFTERNOON

P.M.

12:15 ROUND TABLE LUNCHEONS

1:30 Visit scientific and technical exhibits

2:00 CONVULSIVE DISORDERS

A. B. Baker, Minneapolis

William R. Heilig, St. Paul

3:30 Visit scientific and technical exhibits

4:00 FERTILITY AND STERILITY

Methods of Birth Control

Alan F. Guttmacher, New York

Induction of Ovulation in the Treatment of Infertility

William N. Spellacy, Minneapolis

TUESDAY EVENING

7:00 ANNUAL BANQUET

Reception

Presentations

Entertainment, Dancing and Late Evening

Buffet

WEDNESDAY MORNING, MAY 17, 1967

A.M.

9:00 Socio-Economic Discussion —

Round Table Luncheons

MONDAY — 12:15 P.M.

The Hearing Aid Problem

Joseph H. Leck, Duluth — leader

Craig Linnell, Ph.D., St. Paul

Dialysis in the Community Hospital and the Home

J. C. Hunt, Rochester — leader

Donald A. Duncan, Minneapolis

Fred L. Shapiro, Minneapolis

W. J. Johnson, Rochester

Mr. Harris W. Feldick, Osage, Iowa

Cancer Chemotherapy

B. J. Kennedy, Minneapolis — leader

Harry F. Biesel, Rochester

John H. Brown, Minneapolis

DULUTH

Ongoing Coronary Disease

Carlos E. Harrison, Jr., Rochester — leader
Stephen M. Ayres, New York
Wilbert J. Henke, St. Paul
Harold Katkov, Minneapolis

Field Diagnosis in Athletic Injuries

Edward D. Henderson, Rochester — leader
E. N. Nelson, Minneapolis
W. E. Proffitt, Minneapolis

Annual Physical — Why?

A. Cabot Wohlrabe, Minneapolis — leader
Karl W. Anderson, Minneapolis

The Neuter Sex

Valentine O'Malley, St. Paul — leader
and others

TUESDAY — 12:15 P.M.

Drug Incompatibilities

Raymond N. Bieter, Minneapolis — leader
Edward A. Carr, Jr., Ann Arbor, Michigan

Erythroblastosis

Peter J. Bartzen, Duluth — leader
John M. Bowman, Winnipeg
R. F. Fricson, Winnipeg
J. E. Wall, Duluth
Donald Larson, Duluth
Arthur C. Aufderheide, Duluth
Glen E. Holt, Duluth

(Limited to participants in self-study course)

Diagnosis of the Unconscious Patient

A. B. Baker, Minneapolis

The Thrombosed Hemorrhoid

William C. Bernstein, St. Paul — leader
R. J. Spencer, Rochester
John V. Thomas, Duluth

Multiple Pregnancy

Alan F. Guttmacher, New York

Treatment of Duodenal Ulcers

Owen H. Wangenstein, Minneapolis — leader
James C. Cain, Rochester

Program Highlights

- ... A unique seminar experiment on erythroblastosis fetalis open to all physicians attending the meeting, including those who did not register for the pre-seminar mailings.
- ... A series of eleven 5 minute "How To Do It" talks on such topics as "The Buzzing Ear," "The Bloody Nose," and "Painful Feet."
- ... An outstanding array of guest physicians — listed alphabetically:
 - Dr. Stephen M. Ayres of New York City, New York
 - Dr. John M. Bowman of Winnipeg, Manitoba
 - Dr. Edward A. Carr, Jr., of Ann Arbor, Michigan
 - Dr. R. F. Friesen of Winnipeg, Manitoba
 - Dr. Alan F. Guttmacher of New York City, New York
 - Dr. Thomas E. Starzl of Denver, Colorado
- ... Some friends from the American Medical Association
 - Dr. F. J. L. Blasingame
 - Reverend Paul B. McCleave
- ... Prominent lay speakers —
 - Mr. Jerome T. Bieter of Minneapolis
 - Mr. Jerre Logan of St. Paul
 - Mr. Harris W. Feldick of Osage, Iowa
 - Mr. Burr B. Markham of Minneapolis

Derivatively Speaking

Syphilis — from Syphilus, the name of a shepherd infected with the disease in the poem of Fracastorius (1530). Derived perhaps from Greek syn (together) plus philein (to love).

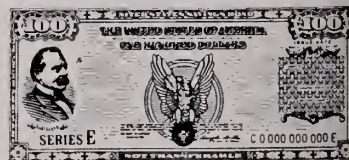
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Vital Records

Minnesota Vital Records

1967 Revision

A. B. ROSENFELD, M.D.*
ROBERT W. HILLER**
Minneapolis, Minnesota

REVISED FORMS for recording births, deaths, and fetal deaths developed by the Minnesota State Board of Health were introduced January 1, 1967. Major revisions of vital records occur approximately every ten years to coincide with the revised recommendations of the United States Public Health Service on the content of vital records. These recommendations to the states, known as the "standard certificates," along with the international classification of diseases, are the two most important instruments for achieving the nationwide comparability and consistency that are so essential in the interpretation of vital statistics data.

A great deal of study and planning have gone into the 1967 Minnesota revision. The topic of standard certificates appeared on the 1962 agenda of the biennial Public Health Conference on Records and Statistics, held in Washington, D. C. Since that time, research organizations, medical societies, hospitals, administrative organizations, law enforcement agencies, and many other groups have been contacted for suggestions and recommendations. State and local registrars of vital statistics, statisticians and other consultants served on study committees to develop specific recommendations to the United States Public Health Service on content and format.

Additional work was required to adapt

these standard certificates to Minnesota laws and practices. Valuable assistance and advice was obtained from a special subcommittee of the Minnesota State Medical Association's committee on obstetrics, gynecology, and maternal health, which included representatives from the Council of the State Medical Association, Academy of General Practice, Department of Obstetrics, University of Minnesota Medical School, and the Minnesota State Hospital Association. Additional assistance and advice were obtained from local registrars, county coroners, funeral directors and morticians.

The revised certificates have been approved by the Council of the State Medical Association, as well as by the Committee on Obstetrics and Gynecology and Maternal Health. They are consistent with the United States Public Health Service recommendations and will be easier to complete and certify. The new documents will also be easier to handle and process for statistical and legal purposes.

Birth Certificate

Substantial differences in format exist between the revised Minnesota certificate and the "standard certificate," but all the basic items on the standard form are included. The most notable difference between the revised Minnesota form and the standard form is that, as in the past, there is a supplemental form containing the medical data (confi-

Continued

*Director, Division of Special Services.

**Chief, Section of Vital Statistics Minnesota Department of Health.

dential medical supplement), rather than a single form as recommended by the United States Public Health Service. This decision was made because of the general agreement that the medical portion of the form should be filed not with the local registrar, but directly with the state registrar.

The new form, which is much smaller than the old one, will be easier for the certifier to complete. Among other things, duplicate entries are no longer required since the revised supplement will be a carbon copy of the birth certificate itself, with the medical data appearing on the lower portion. This arrangement will facilitate the processing of the statistical data and the use of such data in the development of national statistics. Items relating to farm residence, usual occupation and kind of business or industry of father, length of pregnancy, use of silver nitrate, date of mother's first marriage, and the presence of a blood factor involved in erythroblastosis fetalis have been deleted. Many "check box" questions have been changed to "open end" questions to permit greater freedom to the certifier in his response.

Attention should be called to the addition of one item, namely, the name of the certifier, which is to be printed or typed. The certificate still requires the certifier's signature, but a printed name will help avoid the consternation and confusion that occurs at times in the registrar's office when a hieroglyphical signature defies all attempts to break the code.

All birth statistics will now be derived entirely from the medical supplement form. More than ever before, the collection of this essential data depends on the complete and timely filing of the medical supplements. The cooperation of certifiers in the completion and timely filing of the medical supplements will avoid the excessive costs of matching records and duplicating work to obtain basic birth statistics.

Death Certificate

The outstanding features of the revised death certificate include (1) addition of a separate medical certification statement for coroners and medical examiners, and (2)

substantial changes in the arrangement of items. Several items have been deleted, including items on farm residence, length of stay at location of death, and information on the date and major findings of surgical operations. Items have been added for the name of the funeral establishment and the birthplace of the parents.

The present medical certification form was designed primarily for the physician last in attendance. As a general rule, the coroner or medical examiner had to strike out much of the certification statement before signing it. The revised certificate contains two separate certification statements, one appropriate for the physician last in attendance and the other for the coroner or medical examiner.

Items dealing with the date and major findings of operations were deleted because of their marginal value for statistical purposes and because there was some indication that these items interfered with proper certification in Parts I and II. In some instances, for example, information on surgical procedures was omitted when it properly belonged in the certification to avoid erroneous classification of the cause of death.

The question as to whether an autopsy was performed has been expanded to include the question of whether autopsy findings were used in the precise determination of the cause of death. Answers to this question will provide a much improved measure of the reliability of mortality statistics. Because of the time element involved in completing the death certificate as opposed to the time element in obtaining a final autopsy report, it will often be the preliminary and not the final autopsy report that will be considered in the determination of cause of death. The decision to wait for the final autopsy report will depend on the nature of the particular case and on the judgment of the physician as to whether the final report will materially change the diagnosis.

There is a small box in the section of the new form for the medical certification which is to be checked if the diagnosis of cause of death is to be deferred. The certifier will no longer have to write in "diagnosis deferred," "diagnosis pending," or whatever. In addi-

MINNESOTA VITAL RECORDS

MINNESOTA DEPARTMENT OF HEALTH Section of Vital Statistics CERTIFICATE OF LIVE BIRTH

This becomes
a permanent
legal record
when properly
executed.
Please
type, or use
permanent
ink.

LOCAL FILE NUMBER				STATE FILE NUMBER			
1. CHILD - NAME				2a. DATE OF BIRTH			
FIRST MIDDLE LAST				MONTH DAY YEAR 2b. HOUR			
3. SEX	4a. THIS BIRTH SINGLE, TWIN TRIPLET, ETC.			SPECIFY		4b. IF NOT SINGLE BIRTH, BORN FIRST, SECOND, ETC.	
5b. LOCATION OF BIRTH		CITY, VILLAGE OR TOWNSHIP		5c. INSIDE CORPORATE LIMITS SPECIFY YES OR NO		5d. HOSPITAL - NAME	
				(IF NOT IN HOSPITAL, GIVE STREET AND NUMBER)			
6a. FATHER - NAME				6b. AGE (AT TIME OF THIS BIRTH)		6c. BIRTHPLACE (STATE OR FOREIGN COUNTRY)	
FIRST MIDDLE LAST							
7a. MOTHER - MAIDEN NAME				7b. AGE (AT TIME OF THIS BIRTH)		7c. BIRTHPLACE (STATE OR FOREIGN COUNTRY)	
FIRST MIDDLE LAST							
8a. RESIDENCE OF MOTHER - STATE		8b. COUNTY		8c. CITY, VILLAGE OR TOWNSHIP		8d. INSIDE CORPORATE LIMITS SPECIFY YES OR NO	
9. ADDRESS OF MOTHER				10. I CERTIFY THAT THIS CERTIFICATE IS CORRECT			
STREET AND NUMBER POST OFFICE				(SIGNATURE OF PARENT)			
11a. CERTIFICATION I CERTIFY THAT I ATTENDED THE BIRTH OF THIS CHILD WHO WAS BORN ALIVE AT THE PLACE AND ON THE DATE STATED ABOVE				11b. DATE SIGNED		11c. ATTENDANT (M.D., D.O., MIDWIFE, OTHER) SPECIFY	
SIGNATURE							
11d. CERTIFIER - NAME				11e. MAILING ADDRESS			
(TYPE OR PRINT)				STREET AND NUMBER POST OFFICE			
12a. REGISTRAR - SIGNATURE				12b. DATE FILED			

THIS SPACE RESERVED FOR USE OF REGISTRAR

SUPPLEMENTARY INFORMATION							
(This section not to be reproduced on certified copies unless specifically requested.)							
13a. RACE OF FATHER		SPECIFY		13b. RACE OF MOTHER		SPECIFY	
						14. LEGITIMATE SPECIFY YES OR NO	
						15. BIRTH WEIGHT	
16a. EDUCATION OF FATHER		16b. EDUCATION OF MOTHER		19a. PREVIOUS DELIVERIES			
(SPECIFY HIGHEST GRADE COMPLETED)		(SPECIFY HIGHEST GRADE COMPLETED)		HOW MANY OTHER CHILDREN			
ELEMENTARY (0, 1, 2, 3, ... or 4)		ELEMENTARY (0, 1, 2, 3, ... or 4)		ARE NOW LIVING		WERE BORN ALIVE NOW DEAD	
HIGH SCHOOL (1, 2, 3, or 4)		HIGH SCHOOL (1, 2, 3, or 4)		WERE BORN DEAD (FETAL DEATH AT ANY TIME AFTER CONCEPTION)			
COLLEGE (1, 2, 3, 4, 5 or 6)		COLLEGE (1, 2, 3, 4, 5 or 6)					
17. DATE LAST NORMAL MENSTRUATION BEGAN		18a. MONTH OF PREGNANCY PRENATAL CARE BEGAN (1ST, 2ND, ETC.)		18b. NUMBER OF PRENATAL VISITS (0, 1, 2, ETC.)		19b. DATE OF LAST LIVE BIRTH	
MONTH DAY YEAR		IF NONE SO STATE		MONTH DAY YEAR		19c. DATE OF LAST FETAL DEATH	
						MONTH DAY YEAR	

SUPPLEMENTARY INFORMATION FOR MEDICAL AND HEALTH USE ONLY

20. COMPLICATIONS RELATED TO PREGNANCY		DESCRIBE OR WRITE "NONE"		21. COMPLICATIONS NOT RELATED TO PREGNANCY		DESCRIBE OR WRITE "NONE"	
22a. COMPLICATIONS OF LABOR		DESCRIBE OR WRITE "NONE"		22b. WAS LABOR INDUCED IF YES, METHOD			
22c. OPERATIVE PROCEDURES		DESCRIBE OR WRITE "NONE"		23. SEROLOGIC TEST FOR SYPHILIS SPECIFY YES OR NO		24. WAS MOTHER'S BLOOD TESTED FOR RH FACTOR SPECIFY YES OR NO	
25. BIRTH INJURIES TO CHILD		DESCRIBE OR WRITE "NONE"		26. CONGENITAL MALFORMATIONS OR ANOMALIES			
				DESCRIBE OR WRITE "NONE"			

VITAL RECORDS

This becomes a permanent legal record when properly executed. Please type, or use permanent ink.

MINNESOTA DEPARTMENT OF HEALTH Section of Vital Statistics CERTIFICATE OF DEATH

LOCAL FILE NUMBER		STATE FILE NUMBER	
1. DECEASED - NAME FIRST MIDDLE LAST			2. SEX
3. DATE OF DEATH MONTH DAY YEAR			
4a. AGE (IN YEARS LAST BIRTHDAY)	4b. UNDER ONE YEAR MONTHS DAYS	4c. UNDER ONE DAY HOURS MINUTES	5. DATE OF BIRTH MONTH DAY YEAR
6. RACE SPECIFY		7a. COUNTY OF DEATH	
7b. LOCATION OF DEATH (CITY, VILLAGE OR TOWNSHIP)		7c. HOSPITAL OR OTHER INSTITUTION - NAME (IF NOT IN EITHER, GIVE STREET AND NUMBER)	
8. BIRTHPLACE (STATE OR FOREIGN COUNTRY)	9. CITIZEN OF WHAT COUNTRY	10. MARRIED, NEVER MARRIED, WIDOWED, DIVORCED SPECIFY	11. SPOUSE - NAME
12. WAS DECEASED EVER IN U.S. ARMED FORCES SPECIFY YES OR NO	13. SOCIAL SECURITY NUMBER	14a. USUAL OCCUPATION (GIVE KIND OF WORK DURING MOST OF WORKING LIFE, EVEN IF RETIRED)	14b. KIND OF BUSINESS OR INDUSTRY
15a. RESIDENCE - STATE	15b. COUNTY	15c. CITY, VILLAGE OR TOWNSHIP	15d. HUSBAND OR WIFE SPECIFY YES OR NO
16a. FATHER - NAME	16b. BIRTHPLACE (STATE OR FOREIGN COUNTRY)	17. ADDRESS OF DECEDENT STREET AND NUMBER POST OFFICE	
18a. MOTHER - MAIDEN NAME	18b. BIRTHPLACE (STATE OR FOREIGN COUNTRY)	19. INFORMANT - NAME ADDRESS	
20. PART I - DEATH WAS CAUSED BY (ENTER ONLY ONE CAUSE PER LINE (A), (B) AND (C))			IF DIAGNOSIS DEFERRED CHECK BOX
A. IMMEDIATE CAUSE			APPROXIMATE INTERVAL BETWEEN ONSET AND DEATH
B. DUE TO, OR AS A CONSEQUENCE OF			
C. DUE TO, OR AS A CONSEQUENCE OF			
PART II OTHER SIGNIFICANT CONDITIONS			21a. AUTOPSY SPECIFY YES OR NO
21b. IF YES, WERE FINDINGS CONSIDERED IN DETERMINING CAUSE OF DEATH			
22a. ACCIDENT, SUICIDE, HOMICIDE OR UNDETERMINED SPECIFY	22b. DATE OF INJURY MONTH DAY YEAR HOUR	22c. INJURY AT WORK SPECIFY YES OR NO	
IF DEFERRED CHECK BOX	22d. PLACE OF INJURY (AT HOME, FARM, STREET, FACTORY, OFFICE BUILDING, ETC.)	22e. LOCATION STREET OR RFD NUMBER CITY, VILLAGE OR TOWNSHIP COUNTY STATE	
22f. HOW INJURY OCCURRED (ENTER NATURE OF INJURY IN PART I OR PART II, ITEM 20)			
23a. CERTIFICATION - PHYSICIAN I attended the deceased from _____ to _____ and last saw him/her alive on _____. I did not view the body after death. Death occurred at _____ M. at the place and time and on the date stated above and to the best of my knowledge due to the causes stated.		23b. CERTIFICATION - MEDICAL EXAMINER OR CORONER On the basis of the examination of the body and/or the investigation, in my opinion death occurred at _____ M. on the date and due to the causes stated above. The decedent was pronounced dead on _____ M.	
23c. PHYSICIAN - SIGNATURE		23d. MEDICAL EXAMINER OR CORONER - SIGNATURE	
23e. PHYSICIAN - NAME (TYPE OR PRINT)		23f. MEDICAL EXAMINER OR CORONER - NAME (TYPE OR PRINT)	
23g. MAILING ADDRESS PHYSICIAN, MEDICAL EXAMINER OR CORONER		23h. DATE SIGNED MONTH DAY YEAR	
24a. BURIAL, CREMATION, REMOVAL SPECIFY	24b. CEMETERY OR CREMATORY - NAME	24c. LOCATION (CITY, VILLAGE OR COUNTY) (STATE)	
24d. DATE OF BURIAL, CREMATION OR REMOVAL MONTH DAY YEAR	24e. FUNERAL HOME - NAME	24f. FUNERAL HOME - ADDRESS	
26a. DATE FILED BY LOCAL REGISTRAR MONTH DAY YEAR	26b. LOCAL REGISTRAR - SIGNATURE	27. MORTICIAN OR FUNERAL DIRECTOR - SIGNATURE	

MEDICAL CERTIFICATION

SIGNATURE OF SUB REGISTRAR

19

BURIAL OR REMOVAL PERMIT ISSUED

MINNESOTA VITAL RECORDS

This becomes
a permanent
legal record
when properly
executed.
Please
type, or use
permanent
ink.

MINNESOTA DEPARTMENT OF HEALTH Section of Vital Statistics CERTIFICATE OF FETAL DEATH

LOCAL FILE NUMBER				STATE FILE NUMBER			
1. FETUS - NAME FIRST MIDDLE LAST				20. DATE OF DELIVERY MONTH DAY YEAR			
3. SEX		40. THIS DELIVERY SINGLE, TWIN, TRIPLET, ETC.		4b. IF NOT SINGLE DELIVERY BORN FIRST, SECOND, ETC.		50. COUNTY OF DELIVERY	
5b. LOCATION OF DELIVERY CITY, VILLAGE OR TOWNSHIP				5d. HOSPITAL - NAME (IF NOT IN HOSPITAL, GIVE STREET AND NUMBER)			
60. FATHER - NAME FIRST MIDDLE LAST				6b. AGE (AT TIME OF THIS DELIVERY)		6c. BIRTHPLACE (STATE OR FOREIGN COUNTRY)	
70. MOTHER - MAIDEN NAME FIRST MIDDLE LAST				7b. AGE (AT TIME OF THIS DELIVERY)		7c. BIRTHPLACE (STATE OR FOREIGN COUNTRY)	
80. RESIDENCE OF MOTHER - STATE				8b. COUNTY		8c. CITY, VILLAGE OR TOWNSHIP	
9. ADDRESS OF MOTHER STREET AND NUMBER POST OFFICE				10. I CERTIFY THAT THIS CERTIFICATE IS CORRECT (SIGNATURE OF PARENT)			
11. PART I. FETAL DEATH WAS CAUSED BY (ENTER ONLY ONE CAUSE PER LINE FOR (A), (B) AND (C)) A. IMMEDIATE CAUSE				IF DIAGNOSIS DEFERRED CHECK BOX FETAL OR MATERNAL CAUSE SPECIFY			
B. DUE TO, OR AS A CONSEQUENCE OF							
C. DUE TO, OR AS A CONSEQUENCE OF							
PART II. OTHER SIGNIFICANT CONDITIONS OF FETUS OR MOTHER				12. FETUS DIED BEFORE LABOR DURING LABOR OR DELIVERY, UNKNOWN SPECIFY			
140. I CERTIFY THAT THIS DELIVERY OCCURRED ON THE DATE STATED ABOVE AND THE FETUS WAS BORN DEAD				14b. DATE SIGNED		14c. ATTENDANT (M.D., D.O., MIDWIFE, OTHER) SPECIFY	
14d. CERTIFIER - NAME (TYPE OR PRINT)				14e. MAILING ADDRESS STREET OR R.F.D. NO. POST OFFICE STATE			
150. BURIAL, CREMATION, REMOVAL SPECIFY		15b. CEMETERY OR CREMATORY - NAME		15c. LOCATION (CITY, VILLAGE OR COUNTY)		(STATE)	
15d. DATE OF BURIAL, CREMATION OR REMOVAL MONTH DAY YEAR		15e. FUNERAL HOME - NAME		15f. FUNERAL HOME - ADDRESS			
170. DATE FILED BY LOCAL REGISTRAR MONTH DAY YEAR		17b. LOCAL REGISTRAR - SIGNATURE		18. MORTICIAN OR FUNERAL DIRECTOR - SIGNATURE			
SUPPLEMENTARY INFORMATION (This section not to be reproduced on certified copies unless specifically requested.)							
190. RACE OF FATHER SPECIFY		19b. RACE OF MOTHER SPECIFY		20. LEGITIMATE SPECIFY YES OR NO		21. BIRTH WEIGHT	
220. EDUCATION OF FATHER (SPECIFY HIGHEST GRADE COMPLETED) ELEMENTARY HIGH SCHOOL COLLEGE (0, 1, 2, ..., OR 8) (1, 2, 3, 4, 5, 1) (1, 2, 3, 4, 5, 1)		22b. EDUCATION OF MOTHER (SPECIFY HIGHEST GRADE COMPLETED) ELEMENTARY HIGH SCHOOL COLLEGE (0, 1, 2, ..., OR 8) (1, 2, 3, 4, 5, 1) (1, 2, 3, 4, 5, 1)		23. PREVIOUS DELIVERIES - HOW MANY OTHER CHILDREN ARE NOW LIVING WERE BORN ALIVE WERE BORN DEAD (FETAL DEATH AT ANY TIME AFTER CONCEPTION)			
SUPPLEMENTAL INFORMATION FOR MEDICAL AND HEALTH USE ONLY							
24. DATE LAST NORMAL MENSTRUATION BEGAN MONTH DAY YEAR		250. MONTH OF PREGNANCY PRENATAL CARE BEGAN (1ST, 2ND, ETC.) IF NONE SO STATE		25b. NUMBER OF PRENATAL VISITS (0, 1, 2, ETC.)		260. DATE OF LAST LIVE BIRTH MONTH DAY YEAR	
27. COMPLICATIONS RELATED TO PREGNANCY DESCRIBE OR WRITE "NONE"		28. COMPLICATIONS NOT RELATED TO PREGNANCY DESCRIBE OR WRITE "NONE"					
290. COMPLICATIONS OF LABOR DESCRIBE OR WRITE "NONE"		29b. WAS LABOR INDUCED IF YES, METHOD					
29c. OPERATIVE PROCEDURES DESCRIBE OR WRITE "NONE"		30. SEROLOGIC TEST FOR SYPHILIS SPECIFY YES OR NO				31. WAS MOTHER'S BLOOD TESTED FOR RH FACTOR SPECIFY YES OR NO	
32. BIRTH INJURIES TO FETUS DESCRIBE OR WRITE "NONE"		33. CONGENITAL MALFORMATIONS OR ANOMALIES DESCRIBE OR WRITE "NONE"					

SIGNATURE OF SUB REGISTRAR
19
BURIAL OR REMOVAL PERMIT ISSUED

tion to saving time for the physician, the check mark response will facilitate processing in the office of the state registrar because there will be space available on the form for filling in the final diagnosis. In the past, in such instances, the space was already filled with such comments as "diagnosis deferred."

The revised death certificate is almost identical to the United States Public Health Service recommendations, but they were adapted to fit state and local requirements as the result of surveys involving coroners and medical examiners on those aspects of the certificate of direct interest to them. Funeral directors and morticians were also contacted for comments on other aspects of the form.

Fetal Death Certificate

The fetal death certificate, as in the past, is a composite form. It includes information from both the birth and death certificate forms. The major feature of the revision is that the fetal death certificate is a two-page form, rather than a one-page form, with a detachable section. The medical supplement contains a carbon copy of the information on the first page, plus certain medical data on the lower portion, as is true for the birth certificate. The medical supplement to the certificate of fetal death is to be filed with the Section of Vital Statistics of the Minnesota Department of Health, as is the case for the medical supplement to the certificate of live birth.

Interest in fetal death statistics has greatly increased in recent years as medical science has sought to develop a greater understanding of this wastage of human lives that hopefully will lead to preventive measures to decrease the number of fetal deaths. Too, such data are extremely valuable in studies of human fertility. For such data to be meaningful, accurate and complete reporting are essential.

Need for Accurate Vital Records

The word "vital" as used in the terms "vital records" and "vital statistics" reflects a concern with life. Thus, vital records record the beginning and the termination of life. Whether vital records are truly vital,

essential, and important to society and to the individual depends on the uses to which such data are put.

For the individual, they serve as the basic proof of citizenship, age, parentage, etc. enabling the individual to prove entitlement to a great variety of rights and benefits.

There are numerous uses of vital records in the field of public health. Statistical data derived from the records form the basis for efficient planning of many public health programs and activities and assist in the allocation of resources to those areas where the problems are most serious.

Another major use of vital statistics is in the study and analysis of population. Such studies serve as the basis for making current population estimates and projections, which are of great importance throughout the economy, in planning investments in manufacturing plants, highways, public utilities, schools, housing, and many other activities.

Both for public health and for persons engaged in medical science research, a knowledge of the causes of death and factors contributing to those deaths are essential in the determination of needed research that will hopefully prolong life and prevent needless deaths. If more data are required today than in the past it is because more is understood about the relationship between the health of the individual and his socio-economic environment.

Too, modern society is concerned with the prevention of human wastage, whether it is fetal wastage or wastage at some other developmental stage. Where society at one time accepted as inevitable such losses as fetal deaths, maternal deaths, and high infant mortality rates, today it strives to lower these losses to the irreducible minimum.

The achievement of this common goal of public health and the clinical practice of medicine requires a precise knowledge of conditions as they exist. Certifications of births, deaths, and fetal deaths provide the basic data with which to measure these conditions, and the data so provided will be meaningful only to the extent that they are complete and accurate.



Meetings and Announcements

Memory is not wisdom; idiots can by rote repeat volumes. — Yet what is wisdom without memory? — Tupper

APRIL

National Methodist Convocation on Medicine and Theology, April 5, 6, 7, in Rochester, Minnesota. Contact: National Methodist Convocation, P.O. Box 102, Rochester, Minnesota 55901.

Department of Pediatrics at the University of Wisconsin Medical Center, Madison, Wisconsin, will sponsor a three day Postgraduate Conference on "The Mentally Retarded Child," April 6, 7, 8. Contact: Harry A. Waisman, M.D., Joseph P. Kennedy Jr. Laboratory, University of Wisconsin Medical Center, Madison, Wisconsin 53706.

1967 American Industrial Health Conference, April 12-13, New York City, Americana Hotel. Contact: American Industrial Health Conference, 55 E. Washington St., Chicago.

11th Annual Post Graduate Course in Fractures and Trauma, April 19-22, Chicago, John B. Murphy Auditorium at 50 E. Erie Street. Tuition is \$80.00. Contact: James P. Ahstrom, Jr., M.D. Chairman, 55 East Erie Street, Chicago.

18th Hahnemann Symposium: Epithelial-Mesenchymal Interactions, April 17-19, Sheraton Hotel, Philadelphia. Sponsored by the Hahnemann Medical College and Hospital in Philadelphia. Contact: Raul Fleischmajer, M.D.

Minnesota Dermatological Society Meeting, April 1, Veterans Hospital, Minneapolis.

Southwestern Minnesota Medical Society Meeting, April 3, Worthington, 7:00 P.M.

Scott-Carver County Medical Society Meeting, April 4, Wagner Supper Club, Jordan, 7:30 P.M.

Brown County Medical Society Meeting, April 11, New Ulm, 7:00 P.M.

Minnesota Academy of Medicine Monthly Meeting, April 13, Town & County Club, St. Paul, 6:30 P.M.

St. Louis County Medical Society Executive Committee, April 13, 6:00 P.M., St. Luke's Hospital Regular Meeting — 8:00 P.M., St. Luke's Hospital.

Minnesota Academy of Ophthalmology & Otolaryngology Meeting, April 14, Minneapolis Club, Minneapolis, 6:00 P.M.

Minnesota Academy of General Practice House of Delegates Meeting, April 18, Radisson Hotel, Minneapolis, 2:00 P.M.

Rice County Medical Society Meeting, April 18.

Minnesota Academy of General Practice Refresher, April 19-20, Radisson Hotel, Minneapolis, 9:00 A.M.-5:00 P.M.

Minnesota Academy of Occupational Medicine & Surgery Regular Meeting, April 20, Minneapolis Club, 6:15 P.M.

Ramsey County Medical Society Regular Meeting, April 24, 1500 Lowry Medical Arts Building, St. Paul, 8:00 P.M.

MAY

Minnesota State Medical Association Annual Meeting, May 15-16-17, Duluth Civic Auditorium, Duluth, Minnesota.

Hennepin County Medical Society Membership Meeting, May 1, Pick-Nicollet Hotel, Minneapolis, 6:00 P.M.

Southwestern Minnesota Medical Society Meeting, May 1, Worthington, 7:00 P.M.

Scott-Carver County Medical Society Meeting, May 2, Wagner Supper Club, Jordan, 7:30 P.M.

Zumbro Valley Medical Society Meeting, May 3, Plummer Hall, Rochester, 7:00 P.M.

Minnesota Academy of Medicine Monthly Meeting, May 11, Town & Country Club, St. Paul, 6:30 P.M.

St. Louis County Medical Society Meeting, May 11, Executive Committee — 6:00 P.M., St. Mary's Hospital. Regular Meeting — 8:00 P.M., St. Mary's Hospital.

Minnesota Society of Internal Medicine Meeting, May 20, Minneapolis, 9:00 A.M.

Range Medical Society Executive & General Meeting, May 23, Place not determined, 6:00 P.M.

JUNE

A continuation course in Clinical Electroencephalography, June 5-7, Philadelphia, Pa. Sponsored by the American EEG Society and is designed for physicians who have had little or no formal EEG training. Inquiries address to: Donald W. Klass, EEG Course Director, Mayo Clinic, Rochester, Minnesota.



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2. That's when a FILTER QUEEN is needed.



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QUEEN helps purify the air while it cleans!

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The engineers who perfected the FILTER QUEEN machine clearly recognized that all bag-type vacuum cleaners cannot operate with maximum efficiency because they use a porous bag. So, to make suction cleaning action truly efficient, they had to find a way to overcome the leakage in dust and dirt that so often occurs whenever a porous bag is used.

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DOCUMENTARY PROOF: *We would like to send you, with our compliments, an article entitled "Air Hygiene for Hospitals" which appeared in the Journal of the American Medical Association. In this article it is explained what happened to airborne contaminants when a FILTER QUEEN was used in a series of rigidly controlled tests conducted at the Harvard Medical School. Write to Health-Mor, Inc., 203 North Wabash Ave., Chicago, Illinois 60601*

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**Os
frontale**

**Sinus
frontalis**

**Crista
galli**

**Os
nasale**

Lamina cribrosa ossis ethmoidalis

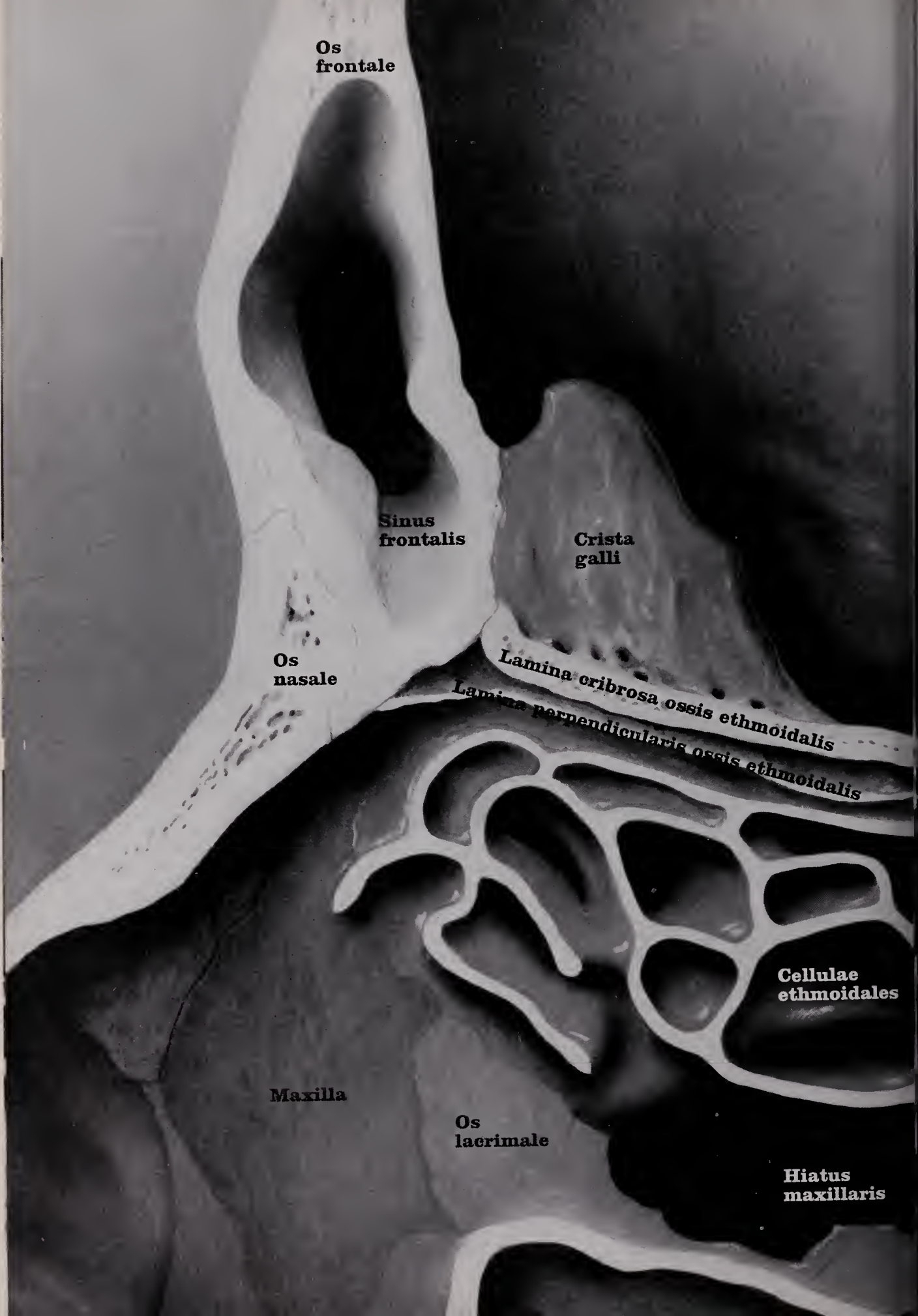
Lamina perpendicularis ossis ethmoidalis

**Cellulae
ethmoidales**

Maxilla

**Os
lacrimale**

**Hiatus
maxillaris**



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It provides two analgesics to relieve pain and discomfort... an effective oral decongestant to reduce mucosal congestion... and an antihistamine to help control allergic manifestations.

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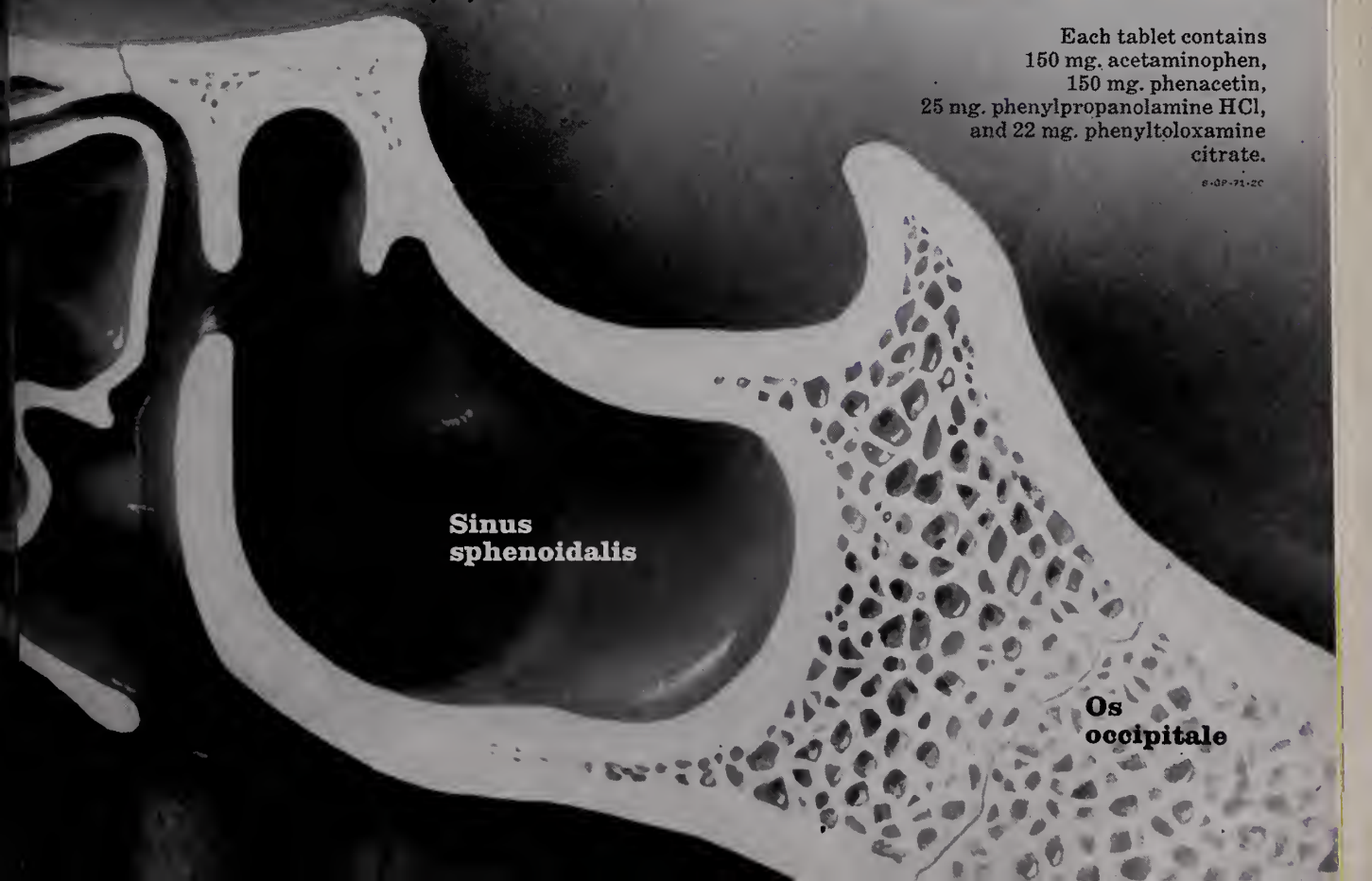


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and 22 mg. phenyltoloxamine
citrate.

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Sinus
sphenoidalis

Os
occipitale

Minnesota Medicine at a Glance

Amebic Abscess of the Liver — Farley and Linner

Page 477

An amebic abscess of the liver is a relatively uncommon disease, but in individuals who suffer from amebic dysentery due to *Entamoeba histolytica* the incidence of abscess in the liver is significant. If an individual has been in a foreign country and arrives home with an illness, this diagnosis should be considered.

Radioactive scan studies of the liver can be a valuable asset in aiding in the diagnosis of liver abscess.

A New Intra-Articular Steroid with Prolonged Anti-Inflammatory Action — Bilka

Page 483

Adrenocorticosteroids have long been known to ameliorate local arthritic manifestations by intra-articular injection. However, the duration of the relief is short, usually less than one month. Triamcinalone hexacetonide is poorly soluble in water, and when injected into joints produces the steroid effect with relief of symptoms averaging three months in duration. The material was used intra-articularly in 125 patients; 92.3 per cent received excellent relief of symptoms.

Duodenal Atresia and Maternal Hydramnios — Barr and Neel

Page 491

Although generally considered to be a surgical emergency requiring the care of a pediatric surgeon, congenital duodenal atresia is shown in this article to be treatable in the community hospital when adequately trained personnel are available. The diagnostic clues of maternal hydramnios, abdominal distention, and absence of or abnormal meconium are emphasized, as well as the classical "double-bubble" radiographic sign. The frequent association of duodenal atresia with Down's syndrome, cystic fibrosis of the pancreas, and congenital abnormalities is emphasized.

Gamma Camera — Loken et al.

Page 497

Many methods for quantitating cerebral blood flow have been attempted previously. This study presents a fresh approach to the problem utilizing a "gamma" scintillation camera with improved electronic circuitry and tubes and a freely diffusible inert indicator which can be administered without significant radiation hazard to the patient. Serial pictures permit estimations of regional cerebral blood flow during uptake and clearance phases of the tracer through the brain. An excellent discussion of the principles and techniques used appears in this report as well as suggestions for further refinements in the procedure. Ultimately it is hoped that this method will be useful in diagnosing and quantitatively evaluating localized abnormalities of cerebral blood flow in stroke and potential stroke patients.

Gastric Ulcers — Benign or Malignant — Bartness

Page 505

Accurate radiological diagnosis of benign and malignant gastric ulcers can be of enormous help in eliminating unnecessary surgery in the former and in avoiding delay in surgery in the latter. Dr. Bartness reports 98 per cent accuracy in this paper and he offers suggestions for identifying the difference.

A Potent Diuretic — Grand Rounds

Page 573

Ethacrynic acid, a relatively new diuretic drug, is readily absorbed in the gastrointestinal tract and has a maximum effect in two hours, with a duration of action extending over eight hours. Though it has a few undesirable effects, it has proven to be effective when all other diuretics have failed. Because of the associated loss of potassium chloride, it is recommended that potassium chloride should be given during the treatment with ethacrynic acid.

Blood Group Antibodies in Prenatal Sera — Polesky

Page 601

Almost 6% of pregnant women have typical blood group antibodies. A knowledge of these antibodies may be useful in preventing hemolytic disease of the newborn and may be essential in preventing transfusion reactions. Routine screening of serum from all pregnant women, Rh+ included, is indicated by the results of this report.

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May 1 *Malabsorption Syndrome*

Dr. Marvin Sleisinger, Gastroenterologist, Cornell University
 Dr. Graham Jeffries, Internist, Cornell University
 Dr. Elliott Weser, Cornell University

May 8 *Upper Gastrointestinal Bleeding*

Dr. James Cain, Internist, Mayo Clinic
 Dr. Lloyd Bartholomew, Internist, Mayo Clinic
 Dr. George Hallenbeck, Surgeon, Mayo Clinic
 Dr. William Summerskill, Internist, Mayo Clinic
 Dr. Erick Wollaeger, Internist, Mayo Clinic

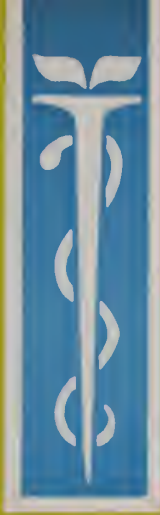
May 15 *University of Minnesota Program*

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STATE MEDICAL ASSOCIATION

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P. W. Harrison, M.D.



114th Annual Meeting Issue
Minnesota State Medical Association

MAY, 1967

Golden Anniversary

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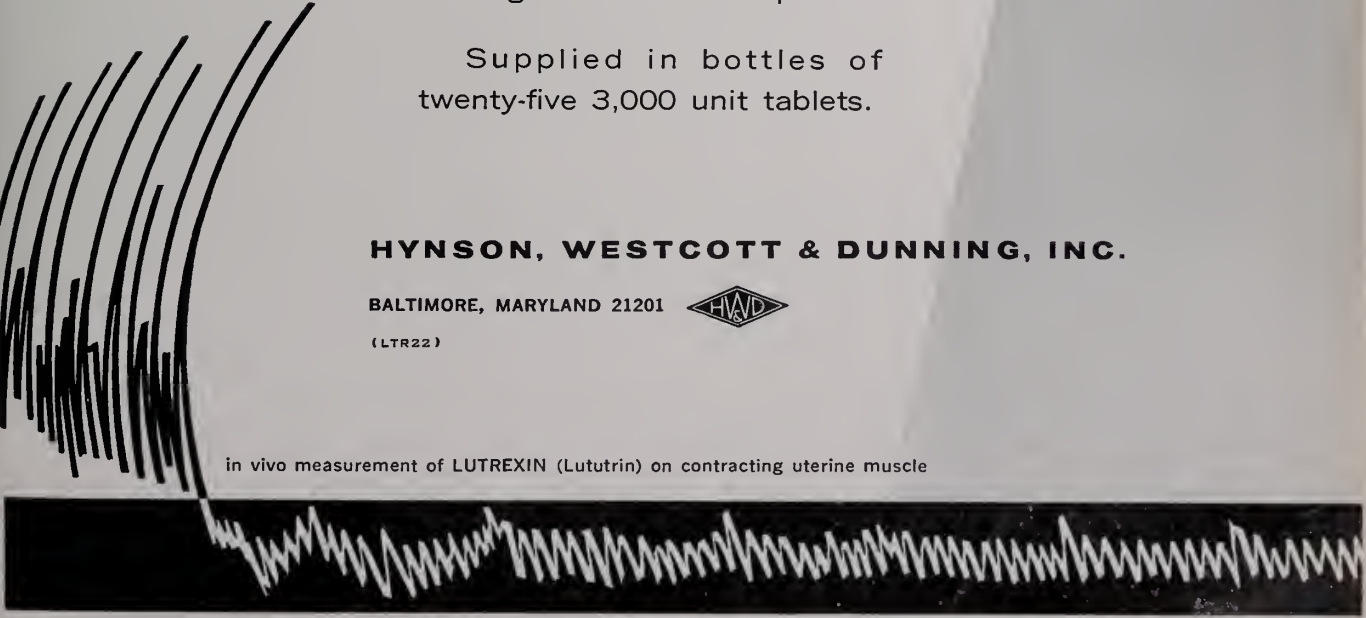
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Worthington, Minnesota

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Picture of bursitis

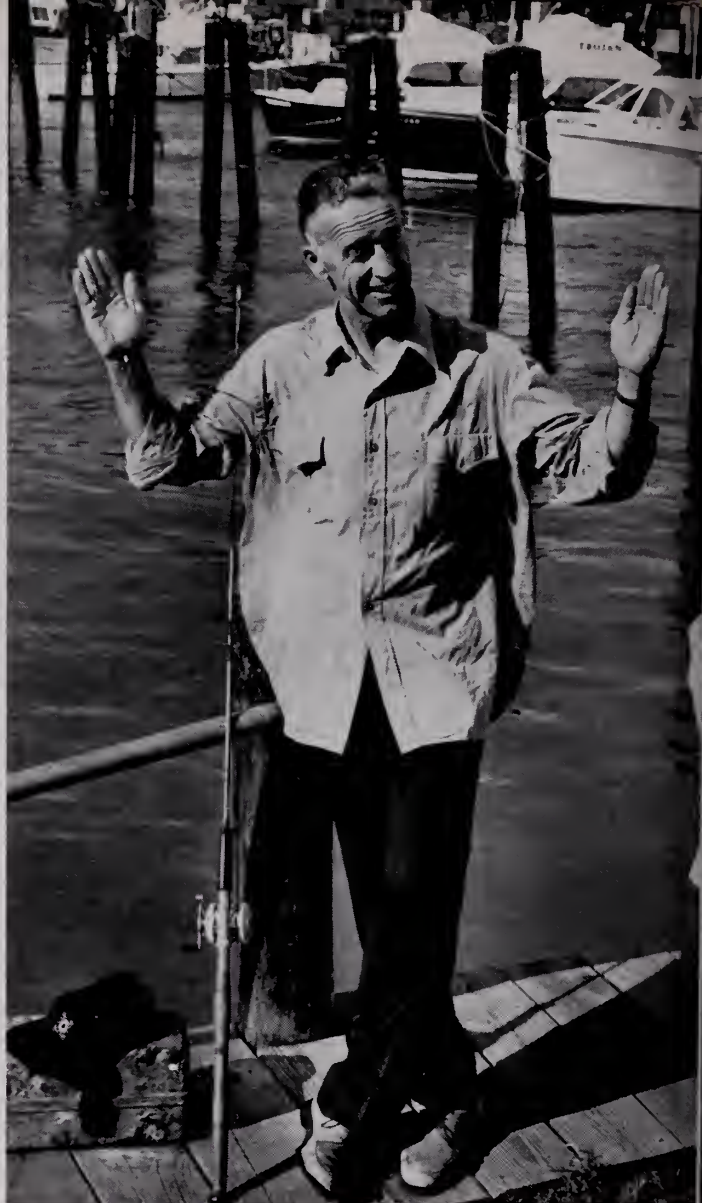
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References: 1. Batterman, R. C., and Grossman, A. J.: *Fed. Proc.* 14:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: *The Pharmacological Basis of Therapeutics*, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Roth, J. L. A., et al.: *Gastroenterology* 44:146, 1963. 4. Conney, A. H., and Burns, J. J.: *J. Pharmacol. Exp. Ther.* 128:340, 1960. 5. Settel, E.: *Clin. Med.* 6:1373, 1959. 6. Berman, H. H., et al.: *Dis. Nerv. Syst.* 25:430, 1964. 7. Darienzo, C.: *Ibid.*, 27:189, 1966.

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President's Letter

ONCE AGAIN, in an abbreviated form, let me call your attention to the fact that we will meet in Duluth in just a few days for the 114th Annual Meeting. This will be a truly historic meeting, especially from the scientific standpoint. An entirely new and exciting type of session awaits your participation. We urge you to attend and give your support. *It's your meeting.* Make it a better one by being there!!!

There are still too many of our own association members, even though their actual numbers are not great, who do not pay their A.M.A. dues. It is true that our combined dues increased this year by \$50.00, and for some of you perhaps more than this. So what?? Ask the average metropolitan worker what his union dues are. Ask him also what his average hourly wage is. Figure out the percentage and see where you stand, even when you pay your whole freight bill as most of us are doing.

Then ask yourself why you are not paying some portion of your dues. We do not have the "check-off" system. We have the "honor" system instead. Not only is it a privilege to belong to such a great organization as the American Medical Association; it is an obligation as well. Maybe you have a personal difference of opinion with some of the established policies. All rules have to be arrived at by compromise, and someone has to give at times, even on a sorely contested point.

True, we've had some crucial dissensions

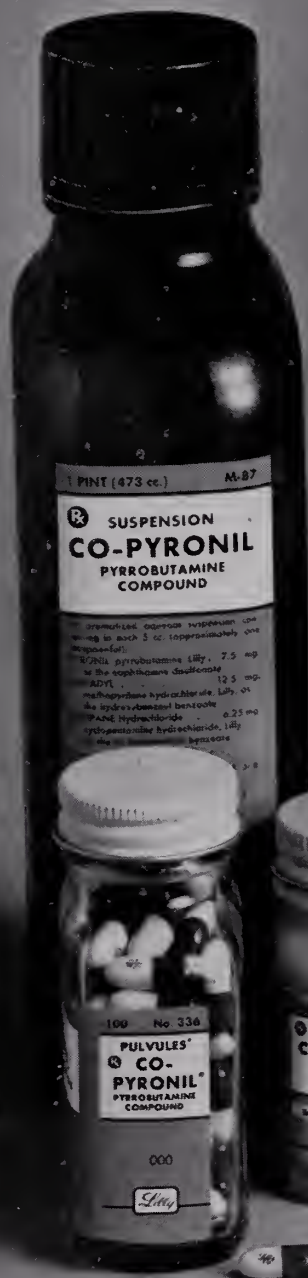
in the past few years. These have been times of crisis for the entire profession; they still are. Is this the time to weaken our structure? I refer you to Dr. Buckley's President's Letter of April, 1966. It is excellent and hits this subject from a somewhat different angle. Your dues *and* participation in the affairs of medicine are sorely needed at this juncture. Now is no time for pettiness, especially in major affairs which affect all of us.

The social planners would like nothing better, believe me, than to have us create schisms amongst ourselves by failing to support our medical organizations: county, state and national. I'm sure many of them are gloating over the arguments and vituperation Medicare has caused between doctors. We must consider the overall effect our words and actions will have on Medicare as a whole and try to bury some of these dissensions in the spirit of genuine compromise. If I sound "preachy," I mean to. I would feel that I had failed as your President, if I did not speak out as I think I ought to.

Once again it is a real pleasure to call to your attention those grand people, the newest additions to our Fifty Year Club, whom we have featured in this issue.

C. G. Sheppard, M.D.

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Neurogenic Tumors in the Head and Neck

LUIS G. KRAUSE, M.D.*
SIMON TOMASISI, M.D.**
Mexico City, Mexico

THE OCCURRENCE of tumors from nerve origin in the head and neck area is rather infrequent,⁷ excluding intracranial and skin tumors. From a total 15,968 new patients studied at the Oncology Institute, 783 belonged to the head and neck service. Within this group, fifteen cases revealed neurogenic tumors, and they are the subject of this communication.†

Clinical Aspects

Incidence and Age

Neurogenic tumors in the head and neck area comprised 1.9% of the cases. Eight occurred in males and seven in females, with an age average of 33.5 years. The oldest patient was 73 years old and the youngest 11 years old.

Symptoms

There are no symptoms that are uniformly present.² In seven cases the initial symptom was a palpable or visible mass; in two cases it was pain and in three cases a combination of both. Nerve paralysis was found in one case, and paresthesia was encountered in two cases along with a palpable mass. Three tumors produced dysphagia and one produced spells of coughing on palpation — all as a result of their peculiar location.

Nerve Trunks

The vast majority of the lesions occurred in a *major nerve trunk*, but in a few cases no connection with a major trunk could be demonstrated.

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†The Medical records of the Hospital of Oncology of the National Medical Center of the Mexican Institute of Social Security were examined from the time the hospital opened in May 1961 through December 1965.

Location

Tongue

The most common location in the mouth is the tongue.³ Neurilemmomas* of the oral portion of the tongue have been described, but their location in the base of the tongue

*See Test Your Word Score Page 687.



Fig. 1 — Eleven-year-old boy with a neurolemmosarcoma of four months evolution in the right parotid area. (Case 2).



Fig. 2 — Thirty-seven-year-old male with a neurilemmoma of three years evolution located in the base of the tongue. Intra-oral view showing elevation of the right side of the base of the tongue. (Case 8).

is a rarity. In this situation early dysphagia is noted plus a visible and palpable mass in the subdigastric area and on intra-oral examination. In this series the only intra-oral case was found in the superior vestibular sulcus. Oral neurilemmomas behave in the same way as neurilemmomas found in other areas.^{4,5}

Parapharyngeal

The parapharyngeal location of the neurogenic tumors is usually associated with the last four cranial nerves, the cervical sympathetic or the parasympathetic nerves; consequently, hoarseness or Horner's syndrome can be found.^{6,7,8,9,10} In our series, direct relation with the vagus nerve could be demonstrated in one case. Since tumors in this location grow in an unyielding space, signs and symptoms of pressure on the neighboring structures can be observed. The larger tumors can displace the main vessels of the neck and encroach upon the alimentary canal.

Lateral Neck and Supraclavicular Region

Localization in the lateral part of the neck and in the supraclavicular area was the most prevalent position in our experience, with six cases in such a location. They were usually asymptomatic except for the visible deformity. When symptoms appear they are due in most instances to intraspinal prolongation of the tumor. These dumbbell type tumors have their origin in one of the spinal nerves, and careful radiological examination often discloses pressure destruction of the cervical vertebrae. One of the cases in this series was of this variety, arising from the second cervical root and encroaching upon the upper cervical spinal cord.

One tumor presented as a swelling in the right cheek. The clinical impression was that of carcinoma of the maxillary antrum, although the radiological study did not show bone destruction. Another case presented as a round mass at the middle third of the sternocleidomastoid muscle.

Histology

Neurilemmoma

There are two different types of nerve tu-

TABLE
Case Reports

Case No.	Age Yrs.	Sex	Date of Study	Clinical Findings	Size of Tumor	Diagnosis Pre-op	Diagnosis Post-op	Aspiration Biopsy	Treatment	Nerve of Origin	Neurological Sequelae	Results
1.-	24	Female	6-2-62	Mass in submental triangle	0.5 cm.	Neurolemmosarcoma	Neurolemmosarcoma	None	Wide local excision	Not identified	None	Alive and free of disease
2.-	11	Male	12-11-62	Mass in right parotid	12 cm.	Adenocarcinoma of parotid	Neurolemmosarcoma	None	Radiation therapy methotrexate	Not identified	None	Dead of disease
3.-	19	Male	1-21-63	Mass in right supraclav.	6 cm.	Neurofibroma	Neurofibroma	Doubtful	Local excision	Brachial plexus	None	Lost to follow-up study
4.-	19	Female	7-8-64	Bulging right soft palate	5 cm.	Neurolipoma	Neurolipoma	Neurolipoma	Local excision lat. cerv. app.	Glossopharyngeal nerve	None	Alive and free of disease
5.-	28	Male	8-6-64	Mass in left parotid	5 cm.	Mixed tumor of parotid	Neurolipoma	None	Superficial parotidectomy	Facial nerve	Left facial paralysis	Alive and free of disease
6.-	34	Female	10-26-64	Mass in left supraclav.	9 cm.	Neurolipoma	Neurofibroma	None	Local excision	Brachial plexus	Radial nerve paresia	Alive and free of disease
7.-	22	Male	2-8-65	Mass in right supraclav.	5 cm.	Neurofibrosarcoma	Neurofibroma	None	Local excision	Brachial plexus	None	Alive and free of disease
8.-	37	Male	2-9-65	Mass in base of tongue	9 cm.	Neurolipoma	Neurolipoma	None	Local excision lat. cerv. app.	Not identified	None	Alive and free of disease
9.-	35	Male	3-26-65	Mass in left lat. neck	13 cm.	Neurolipoma	Neurofibroma	Neurofibroma ? ? ?	Local excision lat. cerv. app.	Cervical sympathetic	Horner's syndrome	Alive and free of disease
10.-	48	Male	7-26-65	Mass in vestibular sulcus (upp)	3 cm.	Accessory salivary gland tumor	Neurolipoma	None	Local excision	Not identified	None	Alive and free of disease
11.-	52	Male	8-24-65	Bulging left cheek	6 cm.	Carcinoma maxillary antrum	Neurolemmosarcoma	Sarcoma	Resection of maxilla	Suborbital nerve	None	Dead of acute pneumonia
12.-	21	Female	8-2-65	Mass in left retro-mastoid	10 cm.	Neurolemmosarcoma	Neurolemmosarcoma	None	Wide local excision	Cervical plexus 2nd. root	Subarachnoid hemorrhage	Surg. death
13.-	47	Female	5-8-65	Mass in sternocleidomastoid	8 cm.	Neurolipoma	Neurolipoma	None	Local excision	Not identified	None	Alive and free of disease
14.-	73	Female	9-27-65	Mass in right supraclav.	8 cm.	Neurolemmosarcoma	Neurolipoma	None	Local excision	Brachial plexus	Radial nerve paresia	Alive and free of disease
15.-	39	Female	11-2-65	Mass in left lat. neck	14 cm.	Neurofibroma	Neurolemmosarcoma	Fluid cells not identified	Local excision	Vagus nerve	None	Alive and free of disease

mors. The first type arises from Schwann's cell and is called neurilemmoma. It is now generally accepted that Schwann's sheath cells give rise to the lesion; but Penfield and Tarlov's^{15,16} opinion that they originate from the fibroblast of the epineurium cannot be discarded and perhaps both theories are partially correct.

The term neurilemmoma has the advantage that it indicates the origin of the tumor and has brought uniformity in terminology, making different terms formerly used obsolete.^{11,17}

The microscopic aspect has two main patterns: the so-called Antoni A and Antoni B types.¹⁸ Type A is easily recognized because of its delicate arrangement of connective tissue and reticular fibers in serpentine and branching formations. The interposed nuclei are seen aligned in rows forming a palisade, and the whole formation assumes an organoid* appearance called the Verocay body. This peculiarity makes it quite easy to confuse these tumors with those of smooth muscle origin.¹⁹ For this reason it is felt that the histologic aspect alone is sometimes insufficient, and before a tumor is classified as neurogenic an effort should be made to show macroscopic evidence of connection with a nerve trunk. The Antoni B type is characterized by loosely arranged cells set haphazardly in a mesh of delicate reticulum fi-

*See Test Your Word Score Page 687.



Fig. 4 — Thirty-nine-year-old female patient with a neurolemmosarcoma of the left vagus nerve. Coughing spells could be induced when the tumor was palpated. She had a full-blown Von Recklinghausen disease. (Case 15).



Fig. 3 — Twenty-one-year-old female with a neurolemmosarcoma of the second cervical root, left side. Notice the tumor mass located between the first two cervical vertebrae showing flecks of calcium. (Case 12).

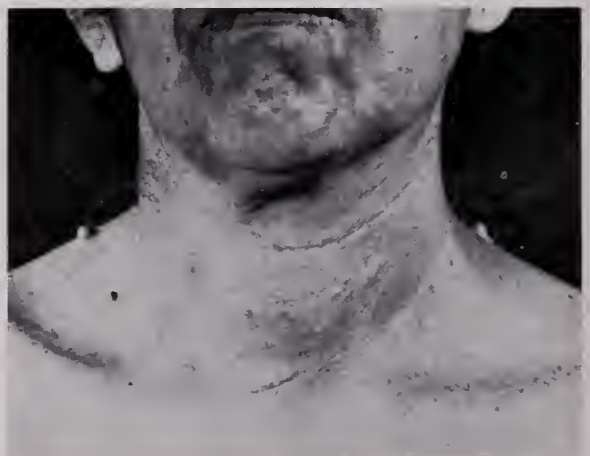


Fig. 5 — Same case as in Figure 4 following surgery.

bers, alternating with cystic spaces. In the capsule of the tumor, nerve fibers belonging to the nerve can be identified.

The malignant variety, the neurolemmosarcoma, is a firm, poorly encapsulated tumor with tendency to invade the surrounding tissues. It has a white greyish appearance, and areas of necrosis and hemorrhage are commonly found. Microscopically there is proliferation of fusiform cells arranged in bands separated by reticular fibers that form a mesh. When some nuclei are found with a tendency to form a palisade, the nerve origin can be assumed more safely.

The largest neurilemmoma measured 8 cm. In one case a typical neurolemmoma alternating with areas of a neurolemmosarcoma was distinctly identified. The largest neurolemmosarcoma measured 14 cm.

Neurofibroma

The neurofibromas are benign, well circumscribed tumors when they arise from nerve ends, and well encapsulated when they arise from nerve trunks. Very often they are multiple, as opposed to the neurilemmomas. The largest neurofibroma measured 13 centimeters in length.

Microscopically, proliferation of nerve fibers along with Schwann's cells can be demonstrated, and the fibrillar loose component is predominant, intermingled with some nerve and reticular fibers. (The neurofibrosarcomas are not discussed here because none were present in these series.)

Coexisting Tumors

In two instances the neck tumor coexisted with a full-blown Von Recklinghausen disease. In another case, the neurilemmoma coexisted with a low-grade liposarcoma of the gluteal region.

There were 10 benign tumors (six neurilemmomas and four neurofibromas) and five malignant tumors (all five neurolemmosarcomas) in the present series.

Diagnosis

When the lesion arises in the lateral portion of the neck, several other pathological conditions must be considered, such as a carotid body tumor, metastatic adenopathy,

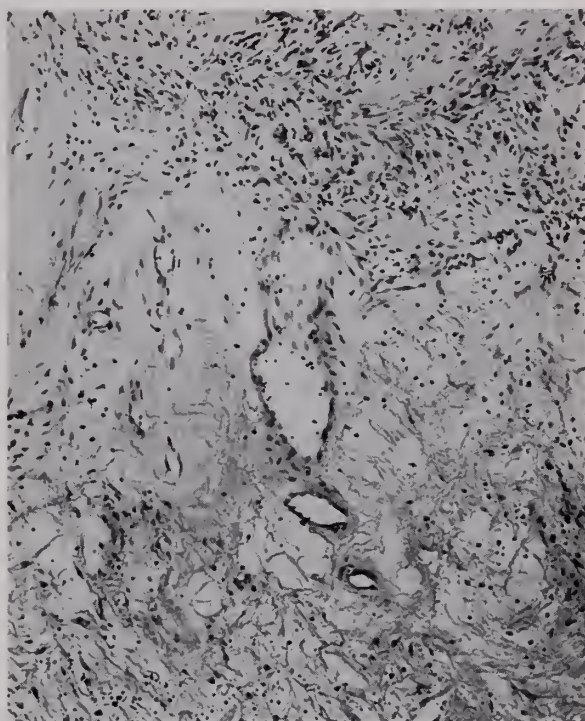


Fig. 6 — Neurilemmoma. Antoni A on the top and Antoni B on the bottom. (Case 8).

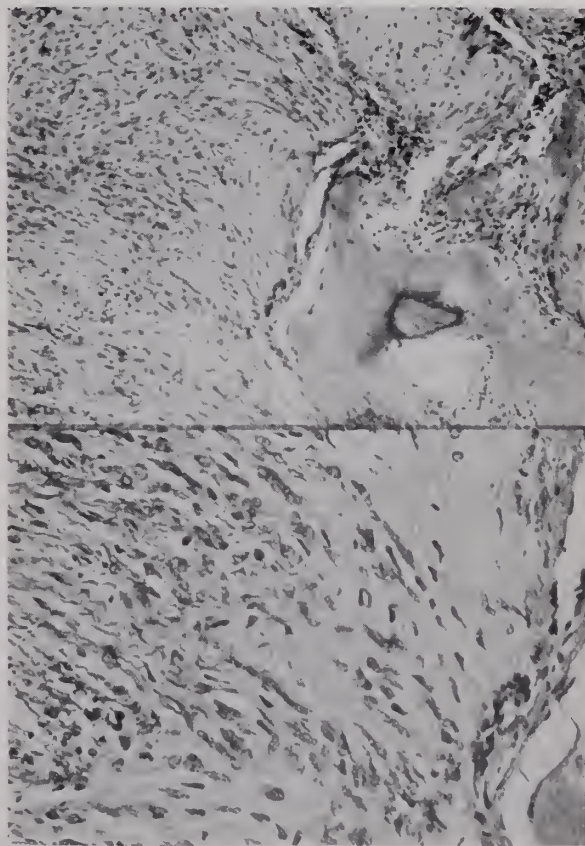


Fig. 7 — Well differentiated neurolemmosarcoma infiltrating bone tissue. Top: low magnification. Bottom: high magnification. (Case 12).

lymphoma, etc.

Of the 15 cases reported here, a correct preoperative diagnosis was made in five cases. The diagnoses made erroneously are indicated in the chart. In three cases the neurogenic nature of the growth was suspected and they were thought to be malignant while they proved to be benign; whereas in a fourth case the lesion was assumed to be benign and was found to be malignant.

In the absence of known tumor pathology elsewhere, the possibility of facing a neurogenic tumor in the head and neck area should be considered whenever a solitary, well limited, partially mobile rubbery mass is encountered in a major nerve trunk. However, a definite diagnosis can not be made short of biopsy or surgical removal of the lesion. We performed aspiration biopsies in five cases; one was reported as doubtful, two as benign neurogenic tumors (both correct), and one as a sarcoma, without stating the possible tissue of origin. In the fifth case 18 cc. of dark-stained fluid were obtained but no cytologic diagnosis could be established. We agree with Harrison and Anderson²¹ that there is a high degree of inaccuracy when the diagnosis is based on a frozen section alone.

Treatment

If the lesion is small and easily accessible a biopsy is not necessary and resection of the tumor can be both diagnostic and therapeutic. We believe resection is indicated in slow-growing benign lesions because of the pressure symptoms that are likely to occur and because of the cosmetic deformity.

All cases in this series were treated surgically. Only two cases had received previous therapy. One case had received radiotherapy without previous tissue diagnosis and the other had had local excision of the tumor.

We agree with Slaughter¹ and others that the cervical external approach is the best. Only small, easily accessible and submucosally located lesions should be removed by the intra-oral route. The external approach offers good exposure, easy control of bleeding, preservation of the immediate surroundings (especially of the nerve that has given

birth to the tumor); and the fact that the mucosa remains untouched affords a non-contaminated operative field minimizing the chances of infection.

When dealing with a benign lesion, the experience to date indicates that local excision of the tumor is curative therapy. Even in the occasional case when part of the capsule of the tumor has been left behind in order to preserve the continuity of the nerve fibers running along it, no recurrences have been encountered. This is a far better method than to leave the patient with neurological sequelae for a benign lesion. In order to achieve this, the dissection must be performed with the utmost care, often within the capsule and dissecting parallel to the direction of the nerve fibers. When dealing with a malignant case the dissection must always be done extracapsularly, and at times the surrounding tissue attached to the growth has to be excised en block.

A review of the literature indicates that radiation therapy and chemotherapy are of no value in the treatment of these tumors.

Results

In the present series two out of five malignant cases were considered non-resectable and the patients died 10 and 36 months after the diagnosis was made. One of them had a dumbbell tumor encroaching upon the cervical spinal chord. Two patients are alive and free of disease: one after three years and one after just two months. The fifth case, a diabetic patient, developed acute pneumonia two months after surgery and died of this complication. All benign cases are still alive and free of disease.

Prognosis

In benign cases the outlook is excellent and the chances of recurrence practically non-existent. If no neurological sequelae are left, recovery is complete. In malignant cases the prognosis is guarded except where the lesion is predominantly a benign tumor with only small nests of low-grade sarcoma. The frankly malignant cases invade surrounding structures early in the course of the disease

and curative surgery can seldom be accomplished.

Conclusions

Aspiration biopsy may be helpful in the diagnosis of neurogenic tumors of the head and neck.

Surgical excision through the external cervical approach is the treatment of choice,

with care taken to preserve the neural structures.

Radiological studies are of no value as diagnostic tools, except for confirmation of the presence of a soft tissue mass or vertebral destruction.

Radiotherapy and chemotherapy have no place in the treatment of this lesion.

References

1. Slaughter, D. P. and de Peyster, F. A.: Pharyngeal Neurilemmomas of Cranial Nerve Origin. Medial displacement of the internal carotid artery as a diagnostic sign. *Arch Surg* 59:386, 1949.
2. Putney, F. H., Moran, J. J., and Thomas, G. K.: Neurogenic Tumors of the Head and Neck. *The Laryngoscope* 74:1037, 1964.
3. Stout, A. P.: The Peripheral Manifestations of the Specific Nerve Sheath Tumor (Neurilemmoma). *Amer J Can* 24:751, 1935.
4. Thomas, K. H., and Goldman, H. M.: *Oral Pathology*, Ed. 5, C. V. Mosby Co., St. Louis, p. 1303, 1960.
5. McMillan, D. R.: Neurilemmoma; Report of 3 cases. *Oral Surg* 16:194, 1963.
6. Manning, E. L.: Solitary Neurofibroma Presenting in Pharynx and Neck with Horner's Syndrome. *Arch Otolaryng* 58:740, 1953.
7. Daly, J. J. and Roesler, H. K.: Neurilemmoma of the Cervical Sympathetic Chain. *Arch Otolaryng* 77:262, 1963.
8. Horwich, M., and Howe, P.: Neurilemmoma of the Vagus Nerve in the Neck. Report of two cases. *Brit J Surg* 49:443, 1962.
9. Cranmer, L. R.: Neurofibroma of the Parapharyngeal Space. *Ann Otol* 67:178, 1958.
10. Gore, D. O., Rankow, R. and Hanford, J. M.: Parapharyngeal Neurilemmoma. *Surg Gynec Obstet* 103:193, 1956.
11. Verocay, J.: Multiple Geschwülste als Systemerkrankung am nervösen apparate. *Festschrift für Chiari*, Wein und Leipzig, p. 378, 1908.
12. Murray, M. R. and Stout, A. P.: Schwann Cell Versus Fibroblast as the Origin of the Specific Nerve Sheath Tumor. *Amer J Path* 16:41, 1940.
13. Nageotte, J.: Sheaths of the Peripheral Nerves. Nerve Degeneration. *Cytology and Cellular Pathology of the Nervous System*. Penfield, W., Ed Paul B. Hoeber, Inc., New York. 3:955, 1932.
14. Masson, P.: Experimental and Spontaneous Schwannomas (Peripheral gliomas). *Amer J Path* 8:367, 1932.
15. Penfield, W.: The encapsulated tumors of the Nervous System. *Surg Gynec Obstet* 45:178, 1927.
16. Tarlov, I. M.: Origin of Perineural Fibroblastoma. *Amer J Path* 16:33, 1940.
17. Verocay, J.: Zur Kenntnis der "Neurofibrome". *Beitr Path Anat* 48:1, 1910.
18. Antoni, M. R. E.: Ueber Rückenmarkstumoren und Neurofibrome. *Studien zur Pathologischen anatomie und Embryogenese, Mit Einen Klinischen Anhang*. J. F. Bergmann, München, 1920.
19. Stout, A. P.: *Atlas of Tumor Pathology. Tumors of the Peripheral Nervous System*. Armed Forces Inst Path 31, 1949.
20. Ehrlich, H. E., and Martin, H.: Schwannomas (Neurilemmomas) in the Head and Neck. *Surg Gynec Obstet* 76:577, 1943.
21. Harrison, B., and Anderson, R.: Neurilemmomas of the Lateral Region of the Neck. *Cleveland Clin Quart* 23:275, 1956.

The Frontier Doctor II*

Doctors on the frontier fought Indians, built cabins and roads, and also wrote reports on meteorology and anthropology. They searched the woods and prairies for herbal substitutes for hard-to-get eastern drugs. Between their grueling rides to succor the sick and injured, some of them built laboratories and tried to advance the sum of medical knowledge. They argued for sewage disposal, tried to regulate bawdyhouses, and denounced heavy drinking and the sale of tainted meat. In California mining camps they attempted to stamp out opium smoking among the Chinese. Ranchers and sodbusters cursed doctors who insisted that they abandon wells tainted with typhoid. They resented the doctors' demand that families sick with communicable disease be quarantined. It was not neighborly to let those nice folks down the road suffer with diphtheria without stopping by to bring them a cake and a little sympathy. The doctor had no heart.

— Richard Dunlop: M.D. Doctors of the American Frontier

*See *Minnesota Med.* 50:486, 1967.

The Mithridaticum

Mithridates lived in constant fear of being poisoned, to overcome which, he tested a large number of poisons on criminals and prisoners of war, and took small, increasing doses of poisons and antidotes during the greater part of his life. Today we use the term mithridatism in medicine to denote the insusceptibility to the effects of poison produced by taking a series of gradually increasing doses. . . . When Pompey defeated Mithridates (66 B.C.) he found the prescription for this very complex general antidote, together with other medical manuscripts with the king's body. This famous prescription became known as the Mithridaticum.

The Mithridaticum was improved especially by Nero's personal physicians and its use extended to a great number of ailments. There were two principal formulas named for Nero's physicians respectively, one having fifty-five ingredients, and the other seventy-two. In Nero's time these complex prescriptions became known as Theriacs, the word being derived from the snake called tyrus, the flesh of which was added to the ingredients by Andromachus, Nero's doctor. Directions for making theriacs are to be found in all dispensaries down to those of the 19th century.*

*Thomen, A. A., M.D.: Don't Believe It! Says the Doctor. Blue Ribbon Books, New York, 1935.

What's Your Diagnosis?

A 29-year-old right-handed man was in excellent health until four weeks prior to hospitalization when stiff neck and occipital headache developed. These symptoms would be present for two to three hours, would subside, and would recur approximately three times a week. Two weeks later unsteadiness in walking developed with a tendency to fall to the right. One week prior to his hospitalization nausea and vomiting developed.

On his admission to the hospital, his temperature was 100.2° F., blood pressure 128/80 mm. of mercury, and pulse 72 and regular. No abnormality of the cranial nerves was found except for bilateral early papilledema. There was no nystagmus. He did not have a stiff neck. He had generalized hyperreflexia but the toes turned down on plantar stimulation. Results of the finger-nose and heel-knee tests showed evidence of moderately severe cerebellar ataxia on the right and a minimal amount of cerebellar ataxia on the left. There was some hypotonia on the right.

The hemoglobin measured 14.7 Gm.; leukocytes numbered 6500 with a normal differential cell count. Roentgenograms of the cervical portion of the spinal column and of the head did not show evidence of any abnormality. An electroencephalogram showed delta waves, grade 1 biparietal occipital, maximal on the left, and generalized dysrhythmia, grade 2. Special contrast studies were then performed by a neurosurgeon. What's Your Diagnosis? Turn to page 648.

One sees the past better than it was; one finds the present worse than it is; one hopes for a future happier than it will be. — Mme. d'Épinay

Sedimentation Rate in the Normal Menstrual Cycle or with Oral Contraceptives

THE ERYTHROCYTE sedimentation rate is a commonly used laboratory test. The purpose of this study was to determine if any alterations in the erythrocyte sedimentation rate occurred in women at different times in the normal menstrual cycle or in women who are taking either a combination or a sequential type of oral contraceptive.

Methods and Materials

A fasting antecubital venous oxalated blood sample was drawn from each volunteer at the University of Minnesota Hospitals between 0800 and 0900. The erythrocyte sedimentation rate was determined at 20, 40 and 60 minutes by the method of Westergren.¹¹ In most instances more than one determination was performed on a given woman at different times during the study and she therefore served as her own control. The statistical calculations then involved correlated pairs, and the data were analyzed by calculation of the means, standard errors, student's "t" values, and probable (p) values. If the p value was greater than 0.05 the result was considered to be not significant.

Results

Menstrual Cycle

Eighteen normal women were studied on the fifth and again on the 25th day of a menstrual cycle. Each cycle was a normal ovulatory type as determined by basal body temperature graph. Table 1 shows that the erythrocyte sedimentation rate values are not different at the two test times in these women.

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Combination Oral Contraceptives

Two studies were done with a combination type oral contraceptive which contained 5.0 mg. norethynodrel and 0.075 mg. mestranol.* The first study involved 26 normal women who had an erythrocyte sedimentation rate determination done prior to taking these drugs and then again on pill day 18 to 20 of the sixth cycle of these drugs taken in the usual manner. The results in Table 2 show a significant rise in the erythrocyte sedimentation rate values after taking the drugs.

The next study involved 44 normal women who had erythrocyte sedimentation rate determinations done during the 12th treatment cycle on pill day 18-20. These women received the same drugs. The erythrocyte sedimentation rate results in Table 3 are elevated to the same degree as those listed in Table 2.

Sequential Oral Contraceptives

Twenty-eight normal subjects were tested in the control state and then again on pill day 18-20 of the sixth cycle of the usual sequence of 2 milligrams chlormadinone acetate and 80 micrograms mestranol.** The results of these tests in Table 4 again show that the drugs caused an elevation in the erythrocyte sedimentation rate.

Discussion

Robin Fåhræus in 1918, looking for a new pregnancy test, was the first to observe that the erythrocyte sedimentation rate was elevated in normal pregnancy.³ He noted that the mean erythrocyte sedimentation rate for men was 3.3 mm/hr., for nonpregnant women 7.4 mm/hr., and for pregnant women 44.9 mm/hr. Many studies have since confirmed these observations.^{5,8,10} The erythrocyte sedimentation rate, therefore, must be cautiously used during pregnancy as a laboratory aid to diagnosis and treatment.²

The normal erythrocyte cell membrane contains a glycolipid which decelerates the erythrocyte sedimentation rate and also is

a receptor site for the adsorption of certain plasma proteins called agglomerins which accelerate the erythrocyte sedimentation rate. In general, fibrinogen and the alpha globulins accelerate and albumin decelerates it.^{3,12} The erythrocyte sedimentation rate is also influenced by the erythrocyte concentration. Because the albumin level is de-

TABLE 1
Erythrocyte Sedimentation Rate Values in Millimeters During a Normal Menstrual Cycle (N = 18)

	Day 5			Day 25		
	20 Min.	40 Min.	60 Min.	20 Min.	40 Min.	60 Min.
Mean	1.97	6.33	12.47	2.78	7.31	14.67
Range	1-4	1-15	3-28	1-7	1-23	2-38
S.E.	0.28	0.96	1.85	0.44	1.18	2.06
†	-1.55	-0.64	-0.79			
P	Not significant					

TABLE 2
Erythrocyte Sedimentation Rate Values in Millimeters During the Control Period and Again in the Sixth Treatment Cycle With Norethynodrel and Mestranol* (N = 26)

	Control			Cycle 6		
	20 Min.	40 Min.	60 Min.	20 Min.	40 Min.	60 Min.
Mean	2.54	7.96	16.27	4.04	12.62	23.04
Range	0.5-8	2-30	4-43	2-10	3-27	5-49
S.E.	0.35	1.21	2.24	0.41	1.43	2.46
†	-2.78	-2.48	-2.04			
P	<0.005	0.01	0.025			

*Enovid 5 mg.

TABLE 3
Erythrocyte Sedimentation Rate Values in Millimeters During Cycle Number 12 of Norethynodrel and Mestranol* (N = 44)

	20 Min.	40 Min.	60 Min.
Mean	3.61	11.64	22.30
Range	1-12	4-34	5-58
S.E.	0.32	0.98	1.74

*Enovid 5 mg.

TABLE 4
Erythrocyte Sedimentation Rate Values in Millimeters During the Control Period and Again in the Sixth Treatment Cycle with Chlormadinone Acetate and Mestranol* (N = 28)

	Control			Cycle 6		
	20 Min.	40 Min.	60 Min.	20 Min.	40 Min.	60 Min.
Mean	2.13	8.13	16.0	6.25	16.87	29.87
Range	1-4	4-13	7-27	3-13	12-30	22-41
S.E.	0.35	1.03	2.45	1.09	2.03	2.10
†	-3.58	-3.83	-4.30			
p	<0.005	<0.005	<0.005			

*C-Quens

*Enovid® was generously supplied by the G. D. Searle and Company, Chicago, Ill.

**C-Quens® were generously supplied by the Eli Lilly and Company, Indianapolis, Indiana.

creased and the fibrinogen and alpha globulin levels are increased it is easy to understand why the erythrocyte sedimentation rate is accelerated in pregnancy.⁷

The effect of other female conditions on erythrocyte sedimentation rate is less well known. Wintrobe¹² observed that the erythrocyte sedimentation rate does not change during the menstrual cycle. Hamilton⁵ produced an elevation of the erythrocyte sedimentation rate by injections of estrogen and progesterone but not with chorionic gonadotropin. Because there are currently millions of women taking oral contraceptives and because there have been no previous reports on the erythrocyte sedimentation rate in these women, the present study was undertaken. In this study it was shown that both the combination and sequential type of oral contraceptives elevated the erythrocyte sedi-

mentation rate. This elevation is probably the result of a plasma protein alteration similar to that which occurs in pregnancy.^{1,6} Regardless of the cause, the clinician who uses the erythrocyte sedimentation rate as a diagnostic aid must be aware of the elevating effect of oral contraceptive drugs if the result is to be interpreted properly.

Conclusion

The erythrocyte sedimentation rate was measured in normal women before and during the taking of certain oral contraceptive drugs. These measurements showed no change in the erythrocyte sedimentation rate during the normal menstrual cycle. There was an elevation in the erythrocyte sedimentation rate among those women who took either the combined or the sequential type of the oral contraceptive.

References

1. Donayre, J. and Pincus, G.: Effects of Enovid on Blood Clotting Factors. *Metabolism* 14:418, 1965.
2. Eastman, N. J., Hellman, L. M., and Pritchard, J. A.: *Williams Obstetrics*. Appleton-Century Crofts, New York, p. 240, 1966.
3. Fåhræus, R.: The Suspension-stability of the Blood. *Acta Med Scand* 55:1, 1962.
4. Granzer, E.: Zur frage eines Receptors der Blut Körperchensenkung. I. Isolierung blutsemkungshemmender fakforen aus menschlichen erythrocytenmembranen. *Hoppe Seylers Z Physiol Chem* 332:88, 1963.
5. Hamilton, G. M.: The Erythrocyte Sedimentation Rate in Pregnancy. *J Obstet Gynec Brit Emp* 60: 409, 1953.
6. Layne, D. S., and Meyer, C. J.: Effects of 19-Norsteroids on Plasma-Protein Binding of Hormones. *Metabolism* 14:429, 1965.
7. Mack, H. C.: *The Plasma Proteins in Pregnancy*. Charles C. Thomas, Springfield, p. 34, 1955.
8. Oberner, E.: Erythrocyte Sedimentation Velocity (B.S.R.) in Normal Pregnancy. *J Obstet Gynec Brit Emp* 55:464, 1948.
9. Ruhenstroth, B. G.: Der Mechanismus der Blutkörperchensenkung. XI. Zur frage des supplements der Blutkörperchensenkung. *Klin Wschr* 43:460, 1965.
10. Vellar, O. D.: Blodsenkningsreaksjonen hos arbeids føre Menn og Kuinner. *Nord Med* 70: 791, 1963.
- 11-12. May be secured from the author or the reprints.

Acute Abdominal Syndrome

Goldstone and Le Marquand* described a syndrome observed in 13 European servicemen on duty in West Africa that simulated acute abdominal disease. The condition was characterized by fever, right upper abdominal pain, and muscular rigidity. Symptoms appeared gradually, reaching a peak within a few hours. The pain sometimes spread to the entire right side of the abdomen and loin. Considerable rigidity was present with relatively less tenderness in the painful areas. Usually there was diminished movement of the right side of the chest and diaphragm, occasionally accompanied by shoulder pain. The prognosis was good with a rapid, spontaneous improvement in most cases. Goldstone and Le Marquand concluded that these patients most likely had an abortive form of perinephric staphylococcal infection. They also suggested that cases which simulate a perforated peptic ulcer with negative findings at operation may be similar to those described here.

Durham, Robert H.—*Encyclopedia of Medical Syndrome*
Hoerber Medical Division, Harper and Row, New York

*Goldstone, B., and Le Marquand, H.: *Lancet* 2:267, 1946.

Green Medicinals

Herbs for the Kidneys and Bladder

Ecclesiasticus said: The Lord hath created medicines out of the earth and a wise man will not abhor them. Remedial agents for the kidneys and bladder include basil, cardoon, foxglove, gorse, juniper, leek, pellitory of the wall,* rest-harrow, and watercress.

For anyone with gorse buds on hand the following recipe might be used to advantage:

To Pickle Gorse Buds

Make a strong pickle of white vinegar and salt, able to bear an egg. Stir very well till the salt be dissolved, clearing off the dregs and scum. The next day pour it from the bottom, and having rubbed the buds dry, put them up in a pickle glass, which should be frequently shaken until they sink under it, and kept well stopt and covered. — Acetaria, 1622

*See Test Your Word Score Page 687.

Buckle Up

Following too Closely

The largest single factor contributing to freeway accidents is following too closely. Remember that stopping distances are longer at higher speeds. Following too closely, particularly behind trucks, reduces visibility of signs and traffic ahead. The number of feet for minimum following distance should be twice the miles per hour of speed.

Have a Good Trip

And finally, have a good trip. It takes one-third to one-half less time to travel on freeways. Travel is more economical. Fuel, wear and tear on your car are saved. Freeways are the safest means of motor travel yet devised. The rest is up to YOU.

Accept YOUR responsibility.

Answer to What's Your Diagnosis

(From page 644)

Ventriculography showed dilation of the entire ventricular system down to the middle of the aqueduct, which was displaced upward and forward by a mass in the posterior fossa.

Suboccipital craniectomy was performed. When the dura was opened the cerebellar tonsils were found to be herniated through the foramen magnum, on the right more so than on the left. A large cystic hemangio-endothelioma was found in the right cerebellar lobe.

The Disturbed Patient?

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THE BASIC REQUIREMENT for a good doctor-patient relationship is mutual respect on the part of two mature people, each of whom acts with understanding and sympathy for the human efforts, tribulations, and limitations of the other."¹

Central to the success of any therapeutic effort is a satisfying interpersonal relationship between the doctor and the patient.² Although aware of the rapid advances in technical and scientific knowledge that have allowed the medical professions to prevent, treat, and cure an increasing number of diseases, the suffering patient continues to look to the physician (and other medical personnel) for compassion and understanding as well. When such hopes are not fulfilled, the ensuing disappointment leads to tension in the doctor-patient interaction. If communication breaks down, the patient may seem "disturbed" in the eyes of the medical staff and be referred for psychiatric evaluation.

Illustrative Cases

Case One

A 39-year-old man was hospitalized because of recurrent chest pain. After a gastrojejunostomy elsewhere for peptic ulcer, he had been plagued by pyrosis for the preceding five years. Numerous hospitalizations had been required for relief of pain, and he was currently unable to work. After appropriate studies the diagnosis of diaphragmatic hernia and reflux esophagitis was made.

A psychiatric consultation was requested because of the patient's "psychopathic personality." The request had been precipitated by his recent "unmanageable" behavior.

Before the patient was interviewed, his behavior was discussed with the medical residents and nursing staff. The head nurse stated that he wandered about the halls at night and never seemed to be in bed. Early one morning, after considerable search on the medical floor, he had been located in the basement coffee room. He stated that he had attended early Mass and had stopped there on the way back to his floor. The head nurse, however, was disinclined to believe this "excuse." Furthermore, she was annoyed at his constant complaining of pain and

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wondered why he did not work more. Another nurse and a nurse's aid engaged in caring for the patient were interviewed. Both agreed that he was a "problem" for the reasons stated above, but they knew very little of his medical history, the nature of his pain, or why he seldom seemed to be in his room. One had heard the doctor mention "psychopath," and she knew this was not good. All agreed, however, that he was cooperative and pleasant and that he did not annoy other patients.

The medical resident regarded the patient's pain as mainly organic. When asked about the word "psychopath," he stated that this impression had been garnered from the patient's poor work record over the past five years. This resident was not particularly fond of the patient and was upset over the "management difficulties" he presented. When asked to be more specific, he replied that this was an impression he had received from the nurses and pointed to the recent incident of "lying" about chapel attendance.

The patient was next interviewed. He was upset by the consultation; it seemed to confirm his suspicion that no one believed that he had pain. Being from a poor Illinois farm family, he had worked long, hard hours throughout his teens and had then joined the armed forces, hoping to make the service a career. However, he had been discharged because of a peptic ulcer. Since then he had been unable to hold a steady job because of the chest pain. He had never acted asocially and had no criminal record. Currently, he was depressed over the inability of the medical profession to cure his pain. As for walking in the halls: "Who wouldn't want to get out of these cramped rooms?" He denied any unpleasanties with the nursing staff but was visibly upset by the chapel incident. When asked to produce proof that he had actually attended chapel, he found a nurse who corroborated his story that he had told another nurse where he was going. Finally, a patient was located who had attended chapel with him.

Our opinion was that this patient was not a "psychopath" but rather an introverted, passive, and rather inadequate personality type who was perhaps using the chest pain unconsciously as a means of escaping economic and social competition.

This case illustrates how a breakdown in communication can lead to increasing distrust and hostility between physicians and nurses and their patient. The epithet "psychopath," and indeed the psychiatric referral, would seem to have been a form of punishment for this patient. His poor work record made him suspect in the eyes of a doctor, and his lack of physical passivity cast him as a "management problem" for the nurses.

Case Two

A 37-year-old housewife was hospitalized because of recurrent chest pain of two months' duration. Physical examination and numerous laboratory tests

failed to reveal any structural causes for the pain. During the first two weeks the pain became more intense and required narcotics for relief. The patient had become increasingly uncooperative about further diagnostic procedures, and a psychiatric consultation was requested because of her "hysteria."

The initial interview revealed an angry and depressed patient. She had been hospitalized several times in the past because of neurotic depression, and had been hopeful that physicians at this clinic would not think this pain was "in my head." She stated that the intense pain was abrupt in onset, often causing her to cry out for relief. There had been several arguments with the nurses about her disturbing the other patients, although she felt that others in the four-bed room "carried on more with pain than me." This had culminated by her being moved to a private room. She was incensed over this because she could not afford it, because she thought she was being "picked on," and because no one had explained to her why it was being done. She stated that a physician had told her that when she could control her reaction to pain she would be moved back. She felt much worse than she had on admission and wanted to leave the hospital.

The medical resident stated that the patient was probably a malingerer and, at least, a "hysterical patient." To him she was difficult to manage, overcritical, and always complaining. He regarded her pain as "functional" and defended the transfer to a private room as necessary for the other patients' welfare.

The three nurses intimately involved in this patient's care were next interviewed. Two regarded her pain as imaginary ("all in her head") and were upset that she complained so much about it. They disliked her disheveled appearance; one stated, "She's too fat anyway." When asked about the move to a private room, all agreed that she had not been forewarned. They hoped we would take over her care. As one put it, "I don't even like to go into her room."

Subsequently, the patient agreed to being transferred to the Open Psychiatry Unit. The first few treatment hours were spent allowing her to review the frustrating experiences noted above. Psychosomatic mechanisms were discussed, and an attempt was made to convince her that we believed her pain to be real. During the remainder of her eight-week stay, the patient had little, if any, chest pain, required no narcotics, and was no management problem whatsoever.

This case illustrates how our emotional

reactions to patients and their illness can either hinder or benefit the eventual result of treatment. The patient, being fearful that her physicians and nurses would think the chest pain imaginary, used exaggeration of symptoms and regressive behavior in an attempt to convince them that such was not the case. This was countered by increasing frustration and anger by the medical and nursing staff, to the point that transfer to a new environment and new doctor-patient relationship were necessary in order to help the patient.

Discussion

Not every doctor-patient encounter can be a successful one; not every patient with cancer is cured. Similarly, not every doctor-patient experience will be a happy one; not every patient will have his emotional needs met by a physician (and vice versa). What we have attempted to point out by these two examples is that when the patient seems unreasonable, unmanageable, or uncooperative, a serious attempt should be made to find out why, including a look into the emotional reactions of the medical-nursing staff to that particular patient and his illness.

Each person brings to the doctor-patient relationship his own peculiar attitude toward illness and toward the medical profession. These feelings have been engendered by cultural and socioeconomic backgrounds, personality patterns, and previous life experiences. A situation producing passivity in one patient may cause anger, aggressiveness,

depression, anxiety, regression, or apathy in others. These reactions will, of course, produce different counterreactions in physicians and nurses, depending in turn on their backgrounds. It does little good to treat the "difficult" patient with pompous directives, indignation, or invectives. What is needed is understanding.

Finally, it is important to remember that paramedical personnel take many cues for their own reactions to a patient from the attending physician. No one would consider using the word "cancer" when referring to a particular patient unless the diagnosis was certain. We would make a plea that the same consideration be given for psychiatric designations such as "psychopath," "hysterical," "malingerer," "homosexual," and so on. Such labels conjure up a variety of reactions in the hearers and may do the patient great disservice.

Summary

Two cases have been presented to illustrate how the development of tension between physician (and other medical personnel) and patient can result in a breakdown of communication which may so disrupt the doctor-patient relationship as to impede the successful treatment of the patient. The suggestion is made that a patient's seemingly abnormal responses will appear less abnormal when viewed with greater understanding of the many ways that sick patients, depending on their backgrounds, respond to the stress of illness.

References

1. Blum, Richard H.: *The Management of the Doctor-Patient Relationship*. New York, Blakiston Company, p. x. 1960.
2. Bellville, Titus P.: Interpersonal Distance in Total Patient Care. *Amer J Obstet Gynec* 90:412, 1964.

Surgery in the Bible

Surgery in the Bible is limited to two operations: one by the Lord and one by Abraham.

And the Lord God caused a deep sleep to fall upon Adam, and he slept: and he took one of his ribs, and closed up the flesh instead thereof;

And the rib, which the Lord God had taken from man, made he a woman.

The fool maintains an error with the assurance of a man who can never be mistaken: the sensible man defends a truth with the circumspection of a man who may be mistaken. — De Bruix

An Idea Taking Shape

The suggestion of studying medicine was first presented to me, by a lady friend. She once said to me: 'You are fond of study, have health and leisure; why not study medicine? . . . But I at once repudiated the suggestion as an impossible one, saying that I hated everything connected with the body, and could not bear the sight of a medical book.

I had been horrified during my schooldays by seeing a bullock's eye resting on its cushion of rather bloody fat, by means of which one of the professors wished to interest his class in the wonderful structure of the eye. Physiology, thus taught, became extremely distasteful to me.

So I resolutely tried for weeks to put the idea suggested by my friend away; but it constantly recurred to me.

Other circumstances forced upon me the necessity of devoting myself to some absorbing occupation. I became impatient of the disturbing influence exercised by the other sex. . . . But whenever I became sufficiently intimate with any individual to be able to realize what a life association might mean, I shrank from the prospect, disappointed or repelled.

But the struggle with natural repugnance to the medical line of life was so strong that I hesitated to pass the Rubicon, and fought many a severe battle with myself on the subject.

At this time I had not the slightest idea of how to become a physician, or of the course of study necessary for this purpose. As the idea seemed to gain force, however, I wrote to and consulted with several physicians in various parts of the country, as to the possibility of a lady becoming a doctor.

The answers I received were curiously unanimous. They all replied to the effect that the idea was a good one, but that it was impossible to accomplish it.

If an idea, I reasoned, were really a valuable one, there must be some way of realizing it. The idea of winning a doctor's degree gradually assumed the aspect of a great moral struggle, and the moral fight possessed immense attraction for me.

This moral aspect of the subject was increased by a circumstance which made a very strong impression on me. There was at that time a certain Madame Restell flourishing in New York. This person was a noted abortionist, and known all over the country. She made a large fortune, drove a fine carriage, had a pew in a fashionable church, and though often arrested, was always bailed out by her patrons. She was known distinctively as a 'female physician,' a term exclusively applied at that time to those women who carried on her vile occupation.

The gross perversion and destruction of motherhood by the abortionist filled me with indignation, and awakened active antagonism. That the honourable term 'female physician' should be exclusively applied to those women who carried on this shocking trade seemed to me a horror. It was an utter degradation of what might and should become a noble position for women.

Being at the time a reader of Swedenborg, and strongly impressed by his vivid representations of the unseen world, I determined finally to do what I could to 'redeem the hells,' and especially the one form of hell thus forced upon my notice.*

*Elizabeth Blackwell: *Pioneer Work in Opening the Medical Profession to Women*, London, 1895.

Pheochromocytoma and Ipsilateral Renal Cell Carcinoma

Examination of Important Aspects

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PHEOCHROMOCYTOMA, A GENERALLY histologically benign tumor, causes a malignant hypertension curable by simple extirpation of the tumor, once a diagnosis is established. Thus, awareness of this curable form of malignant hypertension assumes a great deal of importance in our hypertensive workups. Further, this tumor becomes readily identifiable if a minimum of facts are kept in mind. These few facts allow us to quickly evaluate pheochromocytoma as a cause of hypertension and, if it can thereby be eliminated, move on to other causes at once. A discussion of these few facts is the major purpose of this article; a second purpose is the recording of the first case of pheochromocytoma and ipsilateral renal cell carcinoma in the literature.

Clinical Features

Two types of hypertension are recognized: persistent and intermittent. Intermittent hypertension arouses our suspicion from the outset. Typically, the patient will note severe headaches, excess perspiration, and palpitation. Gifford¹ et al. have found that almost all will have at least one of the above complaints. More often than not the patient will be thin and nervous.

Diagnosis

Most patients will be hyperglycemic. Many will have an elevated basal metabolic rate, in spite of a normal protein bound iodine and radioactive iodine uptake. The patient's thyroid is not over-active; the patient simply has hypermetabolism. The intravenous pyelogram is notable for its lack of useful information in many cases.

Physiologic Evidence

The tumor reacts to external stimuli. The most notable is any form of compression;

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therefore, massage of flank and abdomen may cause a rise in blood pressure. Even hyperventilation can cause compression of the tumor.

Provocative Tests

In the normotensive phase the histamine test is used (blood pressure should be below 170/110 for this test). A base line blood pressure is established by performing a cold pressor test: the hand is immersed in ice water and blood pressure is recorded; a diastolic blood pressure rise of 10 to 20 mm. is normal. Histamine 0.05 mg. administered intravenously should produce a 20 mm. systolic and a 10 mm. diastolic rise in blood pressure. Phentolamine (Regitine) must be on hand! In the hypertensive phase, Regitine 5 mg. administered intravenously should cause a 35 mm. systolic and a 25 mm. diastolic fall in blood pressure.

If one becomes suspicious from clinical data, it is worth noting that the above provocative tests take only minutes to perform.

Confirmatory Chemical Tests

The measurement of the 24-hour-free urinary catecholamines* (epinephrine and norepinephrine) and the methylation products of the catecholamines (vanillin mandelic acid and the metanephrines) are most valuable in the diagnosis of this disease.

Diagnosis by Aortography

The aortogram concludes the diagnostic workup. It removes all doubt in questionable cases. More importantly, it localizes the tumor and assists the surgeon by demonstrating the vascular supply. The radiologist will encounter no difficulty with stimulation of the tumor if he keeps an ampoule of phentolamine (Regitine) on hand during the conduct of this examination.

Case Report

A woman was admitted to St. Joseph's Hospital, St. Paul, Minnesota, on 7/28/65 for gross painless hematuria present for the preceding five days.

Past history revealed intermittent hypertension for ten years, often accompanied by severe headache. Palpitation some eight years previously was confused with angina pectoris and resulted in the use of nitroglycerine for a short period of time.

Physical Examination

A white female of 47 was 5'4" and appeared thinner than her 140 lbs. Admission blood pressure was 160/100, but subsequent blood pressures were normal on this admission. Percussion over the flank regions was not painful and no bruit could be heard on auscultation of the flank or back.

Laboratory Studies

The bleeding and clotting times were normal. The fasting blood sugar was 144 mg.%. The sedimentation rate was 10mm/hr. Urine examination was negative for sugar and showed a full field of red blood cells. Urines were negative for acid-fast bacilli and Tbc culture was reported as showing no growth six weeks later.

Diagnostic Studies

The intravenous pyelogram was entirely normal (Figure 1). Cystoscopy on 7/29/65 revealed bloody efflux of urine from the right ureteral orifice and clear urine from the left. Bilateral bulb retrograde pyeloureterograms were normal. Five cc. of 4% silver nitrate were instilled in the right renal pelvis by ureteral catheter, and during the course of the next week the bleeding stopped and the patient was discharged on 8/6/65.

On 9/24/65, the patient was re-admitted to the



Fig. 1 — Intravenous pyelogram showing entirely normal upper urinary tracts.

*See Test Your Word Score Page 687.

hospital with recurrence of gross painless hematuria. On this admission an aortogram was performed and demonstrated a right suprarenal tumor (Figure 2). Note the normal appearance of the kidney on this examination. Blood pressure on this admission was 168/100. Five mg. of phentolamine (Regitine) intravenously dropped the blood pressure to 128/68 in 1.5 minutes. Twenty-four-hour urine for catecholamines showed 570 mcg./24 hours with the normal value being up to 103 mcg./24 hours. The 24-hour urinary vanillin mandelic acid showed 6.5 mg./24 hours with the normal range being 0.7 to 6.8 mg./24 hours.

Operative Findings

Surgical exploration was performed on 9/30/65 with the patient in the supine position. A right subcostal transperitoneal incision was utilized, reflecting the hepatic flexure medially. Dissection of the adrenal tumor was difficult because the tumor infiltrated posterior to the inferior vena cava. A very small portion of the capsule of the tumor could not be excised, since it was fused to the left posterior aspect of the vena cava, between the vena cava and the aorta. The right kidney appeared normal, but because of recurrent bleeding, it was excised along with the adrenal tumor.

Follow-Up of Patient

The postoperative course was one of uneventful

recovery with blood pressures in the normotensive range. The patient was discharged on 10/1/65 and received a course of 20 cobalt treatments to the right renal bed for added insurance. Total dose was 3300 roentgens.

The patient's blood pressure in November 1965, was 120/84 and in December 1965, 130/88. In February 1966, it was 130/80 and in May 1966, 144/94. She was completely without headache or palpitation when last seen.

Pathologic Findings

The Adrenal

Gross appearance revealed a friable, vascular organ. There were necrotic areas and other areas of fibrosis. Microscopic examination showed granular stellate cells. The tumor was well vascularized at the periphery and hyalinized at its center (Figure 3).

The Kidney

The kidney weighed 150 grams. Subcapsular hemorrhage was present in the upper one third. On section, there was a yellow-brown tumor, 2.3 cm. in diameter, and me-

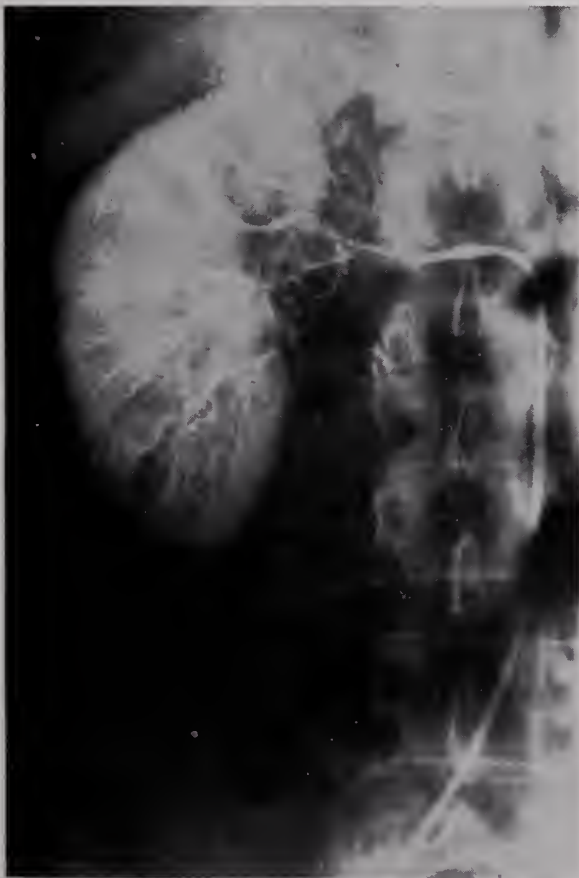


Fig. 2 — Right renal angiogram showing suprarenal tumor but normal kidney. Note especially the upper pole of the kidney where the renal tumor was found.

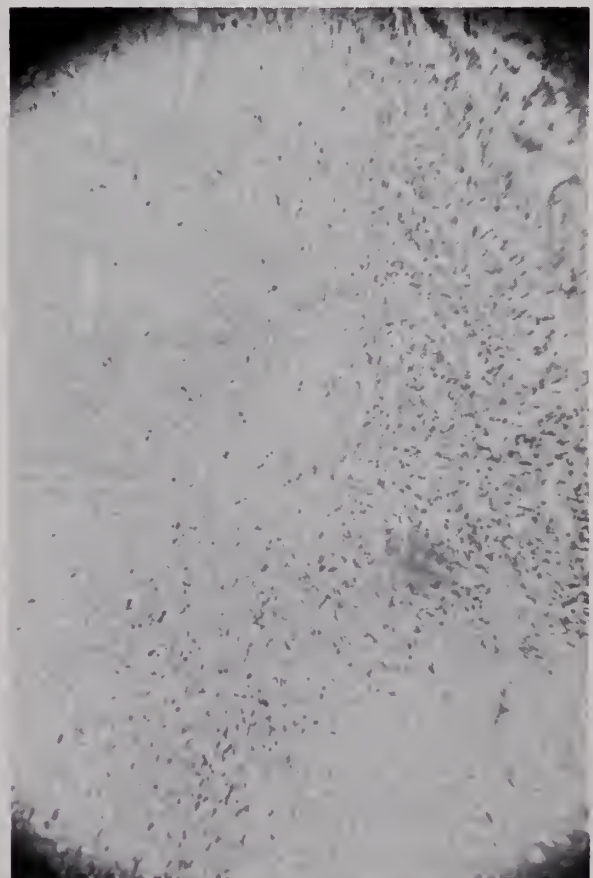


Fig. 3 — Adrenal tumor showing marked hyalinization. This was an old "burned-out" pheochromocytoma. (Approx. 400×)

dial to the superior calyx, eroding into it. Microscopic examination revealed a papillary pattern of cuboidal cells (Figure 4).

Pathology Diagnosis

(1) Pheochromocytoma of right adrenal gland.

(2) Hypernephroma in right kidney.

Discussion

It is imperative to grasp the difference between a maximally and a minimally secreting pheochromocytoma, as described by Crout² et al., as this helps to understand the variations in secretion patterns of catecholamines, vanillin mandelic acid, and the metanephrines.

In the maximally secreting tumor the free catecholamines are converted directly within the tumor to vanillin mandelic acid and the metanephrines (the methylated metabolites of catecholamines); therefore, in the maximally secreting tumor the free catechol-

amines may be normal and the vanillin mandelic acid or the metanephrine values are abnormally high. Moorhead³ et al. have found the metanephrine (methoxycatecholamine) variations to be more reliable than vanillin mandelic acid measurements when free catecholamines are normal.

However, in the minimally secreting tumor the free catecholamines are not being methylated within the tumor and are, therefore, elevated. The vanillin mandelic acid and metanephrine values may be normal.

The case report presented here is one of a minimally secreting tumor since catecholamines were elevated and vanillin mandelic acid was normal. The morphology of the tumor showing marked hyalinization demonstrates the reason for minimal secretion (Figure 3).

One additional point should be made regarding treatment of this tumor: In the intermittent hypertensive patient there are probably no blood volume changes, but in the patient with persistent hypertension, continuous peripheral vasoconstriction from the catecholamines leads to low blood volume, which must be corrected prior to surgery to prevent uncontrollable shock immediately after removal of the tumor. This correction of blood volume can be achieved by maintaining normotensive levels for two weeks prior to surgery with an adrenergic blocking agent such as phenoxybenzamine hydrochloride (Dibenzylin).

A final point to be made in the present case report is the presence of hematuria from the kidney on the same side as the adrenal tumor. Adrenal tumors do not invade the kidney to cause hematuria. Therefore, a second cause for the hematuria must be found. Despite the failure of the aortogram to demonstrate the 2.3 cm. in diameter renal tumor (Figure 2), a fortuitous decision to remove the kidney was made.

Summary

The importance and ease of diagnosis of pheochromocytoma is presented by discussion of the pertinent clinical and laboratory changes in this disease. Special emphasis is placed on the catecholamines and their

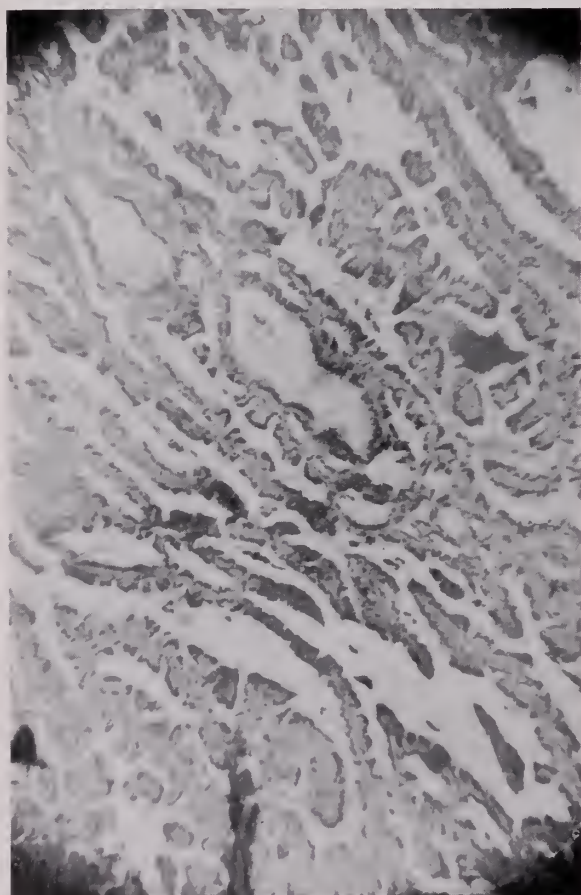


Fig. 4 — Renal cell carcinoma showing its papillary structure. (Approx. 400×)

products of metabolism, since the diagnosis really hinges on these studies. Irreversible shock can occur at surgery. This results from low blood volume which is present in the patient with persistent hypertension through the mechanism of peripheral vaso-

constriction as a result of continuous secretion of catecholamines. Two weeks of an adrenergic blocking agent preoperatively prevents this complication. The first case of pheochromocytoma and ipsilateral renal cell carcinoma in the literature is recorded.

References

1. Gifford, R. W. Jr., Kvale, W. F., Maher, F. T., Roth, G. M., Priestly, J. T.: Clinical Features, Diagnosis and Treatment of Pheochromocytoma: a Review of 76 Cases. *Proc Mayo Clinic* 39:280, 1964.
2. Crout, Richard J., Pisano, John J., Sjoerdsma, Albert: Urinary Excretion of Catecholamines and Metabolites in Pheochromocytoma. *Amer Heart J* 61:375, 1961.
3. Moorhead, Edward L. II, Caldwell, John R., Kelly, Annetta R., Morales, Azorides R.: The Diagnosis of Pheochromocytoma: Analyses of 26 Cases. *JAMA* 196:1107, 1966.
4. Best, H. C., Taylor, N. B.: *The Physiological Basis of Medical Practice*. Williams and Wilkins Co., Baltimore, Md., 1961.

My Get-up-and-Go

How do I know my youth is all spent?
 Well, my get-up-and-go has got up and went.
 But in spite of it all, I'm able to grin,
 When I think of the places my get-up has been.

Old age is Golden, I've heard said,
 But sometimes I wonder, as I go to bed,
 With my ears in the drawer, my teeth in a cup,
 My eyes on the table, until I wake up.

Ere sleep dims my eyes, I say to myself:
 "Is there anything else I should leave on the shelf?"
 And I'm happy to say, as I close the door,
 "My friends are the same — or much, much more".

When I was young, my slippers were red;
 I could kick up my heels right over my head.
 When I grew older, my slippers were blue,
 But still I could dance the whole night through.

Now I am old, my slippers are black;
 I walk to the store and puff my way back.
 But I really don't mind, as I think with a grin,
 Of all the places my get-up has been.

Since I retired from Life's competition,
 I busy myself with Life's repetition.
 I get up each morning and dust off my wits,
 Pick up the paper and read the obits.

If my name is not there, I know I'm not dead;
 So I eat a good breakfast and get back in bed.
 The reason I know my youth is all spent:
 My get-up-and-go has got up and went.

By Mary P. Wilson, Age 83.

The Village Physician and My First Interest in Medicine

It was while I was in Plainfield, before I had studied medicine, that through Dr. Walker I received by baptism in obstetrics. The prospective case was Plainfield's only Magdalene, who lived in a dilapidated house on the outskirts of the town. In preparation Dr. Walker lent me Playfair's *Obstetrics* which, with its classic illustrations, exceeded in interest any detective story. I concealed it in my desk during the day and surreptitiously read its extraordinary revelations at odd times during the school sessions, always expecting that the interesting event which was expected at any moment, would find me unprepared.

On the evening Dr. Walker called for me, he went over the situation as we drove to the house of expectancy, then told me that he had an urgent patient to attend. Would I remain and watch the Magdalene until his return?

Things seemed to me to be developing rather rapidly. It was the first maternity experience for the Magdalene as well as for me, but I expected Dr. Walker to return in time.

To my great relief, at about midnight reinforcements arrived in the person of a thin, aged witch of a midwife carrying a small black bag. About two in the morning we seemed to be reaching a crisis. Convinced that there were fatal complications immediately ahead, I kept close watch on the old woman's face. I was not only completely cooperative but completely nonplussed. Suddenly the old midwife said, "Well, Doc, don't you think we'd better quill her?"

Not knowing what she meant but confident she knew more than I about the procedure, I approved. She took from her small bag a goose quill and a box of snuff. After filling the quill with snuff she inserted one end of it into the patient's nostril, then placed the other end in her own mouth and blew hard. A tremendous sneeze followed and, to my astonishment, the baby arrived precipitately.

Thus encouraged by Dr. Walker, I prepared to enter Wooster Medical School in the spring of 1886.*

*George Crile (1864-1943) in *Why We Became Doctors*, edited by Noah Fabricant, 1954.

MINNESOTA MEDICINE Cover Photographs

In order to encourage more physicians to submit color slides for use on the cover of *MINNESOTA MEDICINE* the competition is being discontinued. The picture editor now invites all physician-photographers to send 35 mm. color slides of suitable subjects for consideration as cover pictures. The format must be horizontal because of printing limitations. Pictures highlighting Minnesota seasons, places, and activities will have an automatic advantage. No limit as to the number of slides sent will be set, but all slides should be individually identified. All slides will be returned. Physicians whose pictures are used as covers will be recognized in *MINNESOTA MEDICINE*. We can use many more pictures than we have received in the past.

|| Headache

A Practical Clinical Approach

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IN ASSESSING patients with headache it is important first to determine which patients require investigation.

Vascular Headache

The most significant is the vascular headache, throbbing at the patient's heart rate. This throbbing may be generalized or local. Vascular headache is due to dilatation of intra or extracranial vessels, presumably due to a histamine-like response. This explains the throbbing nature of the headache in time with the pulse and the increase in headache by bending over, coughing, sneezing, or bowel movement.

Symptomatic vascular headaches are seen with space-occupying lesions such as tumors, cysts, brain abscesses, and hematoma due to local vascular irritation and stretching as well as to increased intracranial pressure. Encephalitis and meningitis also produce vascular headaches, usually with fever. Specific vascular headaches are diagnosed as migraine, Horton's cephalgia, cluster headache, post-spinal headache, postictal headache, temporal arteritis, "seizure equivalent headache," and carotid sheath syndrome.

Migraine

Migraine, by definition, is a unilateral vascular headache, often inherited, which is recurrent and may be preceded by aura. The headache is often tension-triggered and may also be associated with menses due to the tensions concurrent with this, or to the sodium and fluid retention of the premenstrual state. An aura often occurs when intracranial vessels are involved and consists of scintillating scotomata, hemianopsia,* hemihyesthesia or hemiparesis of ten to fifteen minutes duration due to localized vasospasm which precedes the stage of vasodilatation producing the headache. The symptoms, with different episodes, may shift from side to side, and this is reassuring, since if all

*See Test Your Word Score Page 687.

the attacks remain on one side, particularly with aura, consideration of vascular malformation such as arteriovenous malformation or aneurysm must be considered. Unruptured aneurysm can produce migraine syndrome even in the absence of localized cranial nerve palsy. It is said that twenty per cent of patients with migraine have a vascular anomaly.

Therapy of migraine is preferably of a long-term nature. For the actual headache, large doses of aspirin may often help more than opiates. At times, especially with definite tension triggering of the headache, Mebaral 100 mg. and Meproamate 400 mg. allow the patient to sleep off his headache. Long-term therapy such as the use of sedatives, tranquilizers, Dilantin in anticonvulsant doses or Sansert may be helpful.

Horton's Cephalgia

This often occurs at night with conjunctival congestion, tearing and nasal stuffiness and discharge on the side of the headache with visible distention of the superficial temporal artery. Therapy is as above. One may have to try histamine "desensitization."

Cluster Headache

This syndrome is a vascular headache which derives its name from the temporal relationship of the headaches; that is, they occur in clusters or series with periods of freedom from headache of varying length. At times patients describe a seasonal incidence of headaches. Facial pain may occur as a concomitant.

It is said that an ergot drug is almost specific for this syndrome by aborting the series of headaches. It is given twice daily for five days until the headache has cleared and then used on a similar basis intermittently. If the clusters are frequent, then Sansert may be used on a regular basis, but this has the disadvantage of cost as well as the possible side effects of gastrointestinal distress and the recently described complication of retroperitoneal fibrosis.

Post-spinal Headache

This is actually a low spinal fluid pressure headache which on rare occasions may occur

spontaneously, but usually follows spinal tap. In the latter, it is postulated that there is a continued leak of cerebrospinal fluid through the dura at the needle puncture site. Characteristically, the headache is severe and throbbing and is present in the upright position and always relieved virtually completely by lying down. The symptoms last up to two weeks and the treatment consists primarily of bed rest, but vasodilators such as Cyclospasmol and five per cent CO₂ inhalation for five minutes each hour may increase the cerebrospinal fluid pressure. Often where there is an attendant anxiety associated with a spinal tap, one may see tightness develop in the nuchal muscles much as in the muscle contraction headache, and these patients may develop posterior cervical pain which should be treated with heat.

Temporal Arteritis

Temporal arteritis usually occurs in patients over the age of 60 and may be bilateral. The headache is vascular and quite persistent. The superficial temporal artery may or may not be red, swollen or tender. Sedimentation rate is usually elevated. Early diagnosis is important, so that one may prevent the possible complication of blindness. Steroid medication for a six-month period is recommended.

Carotid Sheath Syndrome

Vascular headache and facial pain occur in this condition, at times with the facial pain predominating. The diagnosis is made by demonstrating tenderness over one or both carotid vessels. The condition tends to be self limiting in six to eight weeks; but if the pain is severe, the use of steroids orally may produce fairly prompt relief.

Postictal Headache

This consists of typical vascular headache, often severe following major seizures. Of course the therapy must be directed towards adequate seizure control, but one may use the usual methods of pain relief.

Seizure Equivalent Headache

This headache is more difficult to docu-

ment, but the suspicion of this type of headache is important since therapy is often very effective. The patient complains of vascular headache. On occasion, he may awaken at night with a vascular headache. True vertigo is sometimes present as a symptom unassociated with the headache. There is often a past history of poliomyelitis, rheumatic fever, infectious mononucleosis or some other encephalitic process or a past history of head trauma. Electroencephalogram frequently shows a small amount of random sharp wave activity which may be insufficient to characterize the tracing as abnormal; but occasionally paroxysmal electroencephalogram disturbances are seen. Many patients develop their symptoms after what appears to be relatively insignificant head trauma. Because of the frequent occurrence of electroencephalogram changes and because of the excellent response to Dilantin in anticonvulsant doses it is postulated that the patient may be having subclinical seizures and that a vascular headache follows as a postictal phenomenon.

Tension Headache

The next most important headache because of its frequency is tension headache; or, to use newer terminology, the muscle contraction headache. This typically begins nuchally with tightness, aching and burning and often progresses to a generalized non-specific variable head pain. There is often interscapular pain and burning. Muscle contraction headache is associated with increased activity of the nuchal muscles demonstrated electromyographically. There is diminution of the true resting state. These headaches are tension-triggered, although the patient may or may not be aware of the tension, since frequently recurring tension may be a function of the patient's personality makeup rather than environmental stress. Many patients with this form of distress never seek medical attention, especially if they are aware of the mechanism of the headache. Care must be taken with this type of headache to consider beginning subarachnoid hemorrhage. This characteristically produces vascular headache, but it also produces symptoms due to irritation of the bas-

ilar meninges and therefore causes upper neck pain and ultimately neck stiffness. Another cause of posterior headache is involvement of the greater occipital nerve either spontaneously or due to involvement of the C1-2 nerve roots, which is commonly seen after flexion extension injuries of the cervical spine. Nuchal rigidity of meningeal origin may be differentiated from that of cervical spine or muscular origin by testing the rotation of the neck. Meningeal irritation produces pain and limitation of range of motion with neck flexion, while neck disease produces pain and limitation with rotation as well as with flexion as a rule. If the patient is seen in the throes of a muscle contraction headache, one can often confirm this by twenty to thirty seconds of firm compression of the upper posterior cervical muscles which will produce transient relief of the headache.

Therapy for the individual muscle contraction headache is unrewarding unless it is infrequent. One may give opiates, Darvon, etc., but these are contraindicated in frequently recurring headaches. The therapy of choice, especially with moderately frequent headaches, is daily treatment with Mebaral grains $\frac{3}{4}$ to $1\frac{1}{2}$ grains three times daily, alone or in combination with nicotinic acid 50 mg. three times daily before meals; or with Librium 10 mg. three times a day. This is continued for two to six months and gradually tapered. Aspirin is a useful drug for treating the individual headache. In intractable cases or when one suspects significant psychiatric problems, psychotherapy may be helpful.

Psychogenic Headache

This type of headache is more akin to a hysterical symptom, in which the patient complains of a tight band-like pain around the head with severe pain like a tourniquet or belt being twisted about the head. Other patients complain of a big or heavy head, as if the head is too heavy for the neck or is going to explode. Often these patients will complain of sensitivity to light and of being distressed by noises. The mechanism of this headache is difficult to explain pathophysiologically. These patients often have severe,

frequent, or constant headache. Symptomatic therapy again might be valuable with daytime sedatives or tranquilizers, but more often in these cases one will have to resort to psychiatric referral.

Headache of Pituitary Adenoma

This is orbital, frontal and temporal, and has no particular distinguishing characteristics. It is therefore quite treacherous since it is an early symptom of pituitary gland enlargement. The headache of pituitary tumor is due first to pressure on the diaphragm sella. Afterward the tumor may rupture through the diaphragm and produce a different kind of headache, that of increased pressure or a vascular headache due to local blood vessel changes. Obviously the therapy must be directed to making an accurate diagnosis and then treating the tumor of the pituitary.

Ice Cream Headache

This headache is a referred vagal reaction

to cold and is merely mentioned since it is of no clinical significance.

Miscellaneous Headaches

At times, facial pain is associated with headache; or patients may interpret facial pain as headache. Sinus headache is usually associated with facial pain, but it may also produce vascular headache as in ethmoid sinusitis with inflammatory involvement of the adjacent meninges. Ocular origin of headache is common. Pain due to refractive error is not present in the morning but increases with eyestrain and is present later in the day. The headache of glaucoma, especially acute glaucoma, may produce some problems in differential diagnosis. Trigeminal neuralgia is a recurrent lancinating severe pain, almost always unilateral, the location depending on the branch involved. Herpes zoster of the fifth or seventh cranial nerves may produce head pain as long as two weeks prior to the appearance of the zoster lesion, and for this reason may be difficult to diagnose accurately.

Filling Out Blanks

Voltaire defined a doctor as a man who introduced substances he did not quite understand into bodies he understood even less. This was not meanly said: Voltaire was a lifelong sick man who loved his doctors and owed them eighty-four years of remarkable activity. But for his sake and theirs he reminded them from time to time that they were limited, not absolute, monarchs. . . . The temptation to act like Jehovah must be great, and it is not always resisted, but that is a risk the public must run. It is inherent in the situation.

The sick person wants to believe the doctor omnipotent, and this very confidence helps. But was it not rather the old-fashioned physician who best knew how to enlist that aid? Modern specialization works in the opposite direction. Right now, one physician in three is a full-time specialist, and what he wants to know is "Have you got my disease?" You hope you have, so as to put an end to the shopping around and the interminable waiting and filling out of blanks. You undergo all the tests again at ten to fifteen dollars each — none of the earlier ones are acceptable to the new man — and he puts you through his routine, eager to *finalize the case*.

Jacques Barzun: *When the Doctor Is a Pill* (in *God's Country and Mine*) 1954

*Strange, is it not? that of the myriads who
Before us pass'd the door of Darkness through,
Not one returns to tell us of the Road,
Which to discover we must travel too.* — Omar Khayyam (?-1123)

|| Fluorescence

Selected Medical Aspects

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IN 1942 COONS and his colleagues reported a method whereby antibody could be conjugated to a simple chemical compound, such as fluorescein, without altering its ability to react specifically with antigen. Following this application there has been an ever increasing interest in the use of fluorescein labeled antibody as a method for identifying antigen-antibody reactions as well as localizing the sites of such reactions. In addition, other applications involving the property of fluorescence have been developed in recent years which have added valuable methods for identification and tracing both in clinical practice as well as in research. The present paper will discuss briefly some of the current applications of fluorescence to medicine. However, no attempt has been made to cover the entire scope of this interesting subject.

Fluorescence

Briefly, fluorescence is the emission of light by molecules or atoms following excitation through absorption of light. This phenomenon occurs when a molecule absorbs a quantum of radiation of sufficient energy to alter its electronic distribution. The molecule is then said to be in the excited state. If the excited state is stable and degradation does not occur by collision of the molecule with one of its neighbors, the molecule will return to its ground state by emitting fluorescent radiation. Molecules which possess a conjugated system of double bonds usually have relatively stable excited states and therefore have the characteristic of fluorescence. An example of this type of molecule is fluorescein. In addition, these molecules have small differences between absorption and emission wavelengths due to the small internuclear distance between their

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ground and excited potential energy curves. As a rule the wavelength of the fluorescence or emitted radiation is greater than the absorption or exciting radiation. This is referred to as Stokes' law and is illustrated by fluorescein whose main absorption peak is at 490 m μ and its fluorescence emission at 525 m μ .

Most fluorescent procedures in medicine are relatively simple to perform, involving either direct viewing or simple staining techniques. A difficulty is the high initial cost for the fluorescent microscope with its assorted filters, but many sources are available for adapting existing microscopes to this usage, thus reducing the cost considerably.

Before discussing various techniques employing the application of fluorescent dyes in biological preparations it would seem appropriate to mention several types of natural fluorescence which may occur without prior treatment or application of a fluorochrome.

Tissue Autofluorescence

The majority of human tissues fluoresce blue to bluish-green when viewed with a fluorescent equipped microscope. This fluorescence becomes more intense with the age of the preparation. In addition, various forms of fixation will alter this fluorescence. It is interesting to note that not all organ systems fluoresce with the same intensity; brain and renal tissue have a very strong autofluorescence. The nature of tissue autofluorescence is not understood, many agents both natural as well as drugs having been suggested as contributing to this phenomenon. Vitamin A has been suggested as a possible source of the greenish autofluorescence of skin.² However, no one substance is known to be primarily responsible for autofluorescence in normal tissues.

Porphyrin Molecule

Autofluorescence other than blue may be present in certain pathologic states, most notably porphyria. Runge and Watson demonstrated red fluorescence of the porphyrin molecule in the skin of patients with porphyria.³ Interestingly, this fluorescence was less intense on light-exposed areas of human skin. This fluorescence may also be demon-

strated in normoblasts of patients with porphyria erythropoietica and in the liver in porphyria cutanea tarda. In porphyria if the concentration of uroporphyrin is large the urine will fluoresce when acidified and viewed with a suitable ultraviolet light source.

Various Fungi

This by no means exhausts the list of normal and abnormal states in which so-called autofluorescence is present. It should be mentioned that not all fluorescent tests involve rare diseases or expensive apparatus. The use of a Wood's light [an ultraviolet lamp with a nickel oxide filter producing a wavelength of approximately 3650 Å] has been used for many years as an aid in the diagnosis of various fungus diseases. *Tinea capitis* caused by *M. audouini* and *M. canis* will show this type of fluorescence. *Tinea versicolor* with its yellowish fluorescence and *erythrasma* with a coral red fluorescence are further examples.

Fluorescent Antinuclear Antibody

Antinuclear antibodies found in the IgG, IgA and IgM fractions of serum globulins have been identified in an ever increasing number of diseases demonstrated with the indirect Coons technique. In brief, this procedure involves applying sera, suspected to contain antinuclear antibody activity, to a cellular source of nuclei. After a specified incubation period the cells are washed and fluorescein-labeled antihuman globulin, if human sera are being tested, is applied. This is again incubated, washed and viewed with a microscope which has been fitted with an ultraviolet light source, darkfield condenser and proper filters. If the test is positive one views nuclei with human antibody globulin attached and to which is united antihuman globulin antibody which has been conjugated to fluorescein. It can be seen that the human globulin antibody has a dual function. First it functions as antibody and then as an antigen for the fluorescein-labeled antihuman globulin. This method has been appropriately called the "sandwich technique." This is also known as the indirect method as contrasted with the direct technique. In the

latter, the antisera under study are conjugated to the fluorescein. At present the "indirect" technique is in more common use, for it appears to have greater sensitivity. However, it involves more steps and is harder to control than the "direct" method. The fluorescent dye most often used in this country is fluorescein isothiocyanate, whose molecule has a peak absorption at 490 $m\mu$ and a fluorescent emission at about 525 $m\mu$. Its protein conjugates give off an apple-green fluorescence. It is readily available commercially, both in a free and in a conjugated form. By conjugation is meant the joining of the fluorochrome to the protein (antibody). This must be a stable bond for success, not a simple dye-protein adsorbate which tends to dissociate. The degree to which conjugation affects antibody activity appears to vary with the basic nature of the antibody molecule, its reactor sites, and with other factors.

When viewing these preparations one uses a microscope equipped with an ultraviolet light source and a darkfield condenser. If positive, there is bright apple-green fluorescence observed in the nuclei of the cells being used. In addition, the nuclei appear somewhat enlarged or swollen. In a negative test only the outlines of the nuclei will be seen. There are several commonly observed patterns of nuclear fluorescence: homogeneous, speckling, and nucleolar. In addition, a form in which the fluorescence is found beyond the nuclear membrane has been reported. This last type is stated to be characteristic for systemic lupus erythematosus. At present it seems unwarranted to place emphasis upon the various nuclear patterns in regard to specific diagnoses.

Fluorescent Treponemal Antibody Test

This method makes use of the indirect Coons technique to test for the presence of antibodies directed against *treponema pallidum*.^{*} It is performed in essentially the same manner as the fluorescent antinuclear antibody test with the exception that *T. pallidum* is the antigen instead of nuclear material. If the patient's serum is positive the treponemes will fluoresce and are therefore eas-

ily identified. This procedure has definite advantages over such tests as the *treponema pallidum* immobilization test. First, it is less expensive, not requiring live treponemes, and secondly, one does not have to be concerned with the exact morphological identification of the treponemes. This test is presently referred to as the fluorescent treponemal antibody-absorption test. In this procedure a water soluble extract of Reiter treponemes is employed to remove nonspecific antibodies shared by *T. pallidum* with nonpathogenic treponemes. This has increased the test's specificity.

This discussion by no means exhausts the list of applications of the indirect fluorescent method of protein tracing. It has been applied to studies of bacteria, viruses, and fungi with varying degrees of success and in many instances, equivocal results.

Acridine Orange

Malignant cells show an increase in ribonucleic acid within their cytoplasm as well as large amounts of desoxynucleic acid in their nuclei. The acridine orange method of rapid staining is based upon this fluorochrome's affinity to stain both these proteins. In an alcoholic solution acridine orange binds to nucleic acid by electrostatic linkages and van der Waals forces. When viewed with a fluorescent microscope the cytoplasm of a malignant cell stains brilliant red, while the nucleus stains green to yellow.

Considerable controversy exists concerning the interpretation of findings with this method. Apparently dye concentration as well as pH are important factors. Only with low concentrations of acridine orange do the nucleus and cytoplasm stain differently.

Raskin⁴ in studying 446 cutaneous tumors with acridine orange was able in most instances to differentiate malignant from benign lesions. Due to the fact that many benign cells also show fluorescence to some extent with this method, the examiner must discern whether the cells show abnormal morphology. Therefore, in this method not only fluorescence but morphology must be ascertained regarding the question of malignancy. The acridine orange method has been

^{*}See Test Your Word Score Page 687.

applied to cervical smears and various body fluids.⁵ In the hands of an experienced examiner it does provide a method of rapid screening for malignancy in cytological specimens. However, in all cases the final diagnosis of malignancy rests with the pathologist.

Tetracycline Fluorescence

Tetracycline tends to localize in certain tissues such as teeth, bone, tumors and ulcers, fluorescing a brilliant yellow when viewed with an ultraviolet light source.

The deciduous teeth of children may be stained with tetracycline given to the pregnant mother during or after the fifth fetal month, an effect apparently related to total dose of the drug and not to the duration of therapy.⁶ The color of the teeth will vary from yellow to a dirty brown. Under Wood's light, teeth so affected will fluoresce yellow. The drug apparently forms a chelate with calcium, and because calcium turnover in teeth is slight, this staining remains indefinitely.

Growing or calcifying bones show an uptake of tetracycline, which can occur in normal and abnormal bone as well as in osteosarcomas. It has been demonstrated in areas of ectopic ossification as well as ossified areas of osteosarcomas.^{8,9} Following a single dose in dogs, tetracycline may remain in bone up to one year.⁷ Due to the fact that there is a turnover in bone calcium, this drug will gradually be lost from bone. Bone which has been formed prior to tetracycline administration has only a blue-autofluorescence while bone formed in the presence of tetracycline will fluoresce yellow. This fluorescence tends to appear in any tissue when calcification is occurring.

Various tumors may show fluorescence following tetracycline administration. This localization of tetracycline has been demonstrated in cutaneous as well as internal malignancies. In 1957 Rall et al.¹⁰ demonstrated that carcinomas would fluoresce under ultraviolet light if the patient had received tetracycline. Since then, tumor affinity for this drug has been demonstrated in many ma-

lignancies. Berk and Kantor¹¹ used tetracycline fluorescence of gastric sediment as a test for carcinoma of the stomach. Lipnik¹² reported a method of rapid screening of cutaneous malignancies which involved the application of a demethylchlortetracycline solution to the suspected lesions. A yellow-green fluorescence resistant to 4.9% trichloroacetic acid develops in the lesion when viewed with ultraviolet light. The author has found this drug to cause fluorescence in basal cell epitheliomas, squamous cell carcinomas, and malignant melanomas when patients have had as little as a single 1000 mg. oral dose the day prior to removal of the tumor. With respect to squamous cell carcinoma one must interpret these results with caution, for this tumor may show autofluorescence without prior tetracycline administration.¹³ This fluorescence is restricted to the necrotic ulcerated areas of the lesion.

Loo et al.¹⁴ found that in mouse tumors the fluorophore is apparently a tetracycline-peptide complex that dissociates readily in acid media. Dubuy and Showacre¹⁵ reported that tetracycline combined specifically with mitochondria of animal cells. The exact nature or mechanism of tetracycline's affinity for tumor tissue has not as yet been elucidated. Many of the reports concerning this drug's affinity for tumor tissue have been conflicting and any practical application must await further investigation.

Thioflavine-T and Amyloid

The demonstration of amyloid by histochemical techniques is often difficult. Methods in common use include metachromasia with Congo red and crystal violet, dichroic* birefringence with Congo red, and the fibrillar structural pattern viewed with the electron microscope. Results obtained with Congo red and crystal violet are often equivocal. Both methods may produce false negative as well as false positive results. In addition, the crystal violet method must be viewed soon after preparation, for fading of the reaction occurs rapidly. Of the methods mentioned thus far, Congo red dichroic birefringence is most specific and produces the fewest false-positive results.

Another method for amyloid demonstra-

*See Test Your Word Score Page 687.

tion has recently been described by Vassar and his associates, involving the fluorochrome thioflavine-T.¹⁶ Amyloid, when stained with this substance and viewed with a fluorescent microscope, will fluoresce brilliant yellow. This technique has certain advantages over the other methods for demonstrating amyloid deposits. First, it is far more sensitive and gives results more consistently positive.¹⁷ Secondly, the deposits are more sharply defined with this method and much smaller deposits may be identified. False positive results do occur, such as the staining of keratin; however, these are usually easy to identify. This method is of definite value in demonstrating amyloid, especi-

ally in rapid screening. It is best, of course, to also use one or more of the other methods in conjunction with thioflavine-T.

Conclusion

Many new techniques involving fluorescence have been introduced in recent years. Numerous other fluorescent applications of interest exist, such as fluorescein and rhodamine B for reticular fibers and osteoid tissues, acriflavine for elastic fibers, and acridine orange or Atabrine for mucin, to mention just a few. The use of fluorescent microscopy has provided an interesting as well as helpful tool in both routine pathologic diagnosis and research.

References

1. Coons, A. H., Creech, H. J., Jones, R. N., and Berliner, E.: The Demonstration of Pneumococcal Antigen in Tissues by the Use of Fluorescent Antibody. *J Immun* 45:159, 1942.
2. Cornbleet, T., and Popper, H.: Properties of Human Skin Revealed by the Fluorescence Microscopy. *The Normal Skin: Vitamin A Content of the Skin. Arch Derm* 46:59, 1962.
3. Runge, W., and Watson, C. J.: Experimental Production of Skin Lesions in Human Cutaneous Porphyria. *Proc Soc Exp Biol Med* 109:809, 1962.
4. Raskin, J.: Fluorescence Microscopy in the Diagnosis of Cutaneous Malignancy. *Arch Derm (Chicago)*, 82:965, 1960.
5. Dart, L. H., and Turner, T. R.: Fluorescence Microscopy in Exfoliative Cytology. *Lab Invest* 8:1513, 1959.
6. Wallman, I. S., and Hilton, H. B.: Teeth Pigmented by Tetracycline. *Lancet* 1:827, 1962.
7. Boyne, P. J., and Miller, C. W.: A Study of Tooth Development by Tetracycline-induced Fluorescence. *J Dent Res* 40:1079, 1961.
8. Peterson, W. C., Jr., Carlson, C. H., Singer, L., and Armstrong, W. D.: Analysis of Ectopic Bone in Osteoma Cutis. *Arch Derm* 88:540, 1963.
9. Owen, L. N.: Fluorescence of Tetracyclines in Bone Tumours, Normal Bone and Teeth. *Nature* 190:500, 1961.
10. Rall, D. P., Loo, T. L., Lane, M., and Kelly, M. G.: Appearance and Persistence of Fluorescent Material in Tumor Tissue After Tetracycline Administration. *J Nat Cancer Inst* 19:79, 1957.
11. Berk, J. E., and Kautor, S. M.: Demethylchlor-tetracycline-Induced Fluorescence of Gastric Sediment: Use to Differentiate Benign and Malignant Gastric Lesions. *JAMA* 179:977, 1962.
12. Lipnik, M. J.: Rapid Fluorescent Screening Test for Skin Malignancy. *Arch Derm* 87:575, 1963.
13. Ronchese, F., Walker, B.S. and Young, R. M.: Reddish-Orange Fluorescence of Necrotic Cancerous Surface Under Wood Light. *Arch Derm* 69:31, 1954.
14. Loo, T. L., Titus, E. D. and Rall, D. P.: Nature of Fluorophore Localizing in Tetracycline-Treated Mouse Tumor. *Science* 126:253, 1957.
15. DuBuy, H. G., and Showacre, J. L.: Selective Localization of Tetracycline in Mitochondria of Living Cells. *Science* 133:196, 1961.
16. Vassar, P. S., and Culling, C. F. A.: Fluorescent Stains with Special Reference to Amyloid and Connective Tissues. *Arch Path* 68:487, 1959.
17. Hobbs, J. R., and Morgan, A. D.: Fluorescence Microscopy with Thioflavin-T in the Diagnosis of Amyloid. *J Path Bact* 86:437, 1963.

The only freedom which deserves the name is that of pursuing our own good in our own way, so long as we do not attempt to deprive others of theirs, or impede their efforts to obtain it. Mankind gains more by suffering each other to live as seems good to themselves than by compelling each to live as seems good to the rest. — John Stuart Mill

What the future has in store for you depends largely on what you place in store for the future. — Kalends

Power of Will

Eight years ago I decided to give up smoking, as I had always smoked rather too much. Although I could stop it for a short time, at the end of, say, a month I was only too glad to get back to smoking again, and suffered from deprivation symptoms in the meantime. I therefore decided to try my own method. Having burnt my tobacco pouch and pipe, I leant back in my chair, relaxed my muscles, and thought of sleep — starting with the extremities, fingers, toes, hands, and feet, and reinforcing the relaxation by deep breathing. When in a thoroughly relaxed state, I silently affirmed to myself 'I shall never smoke again; it means nothing to me. I shall feel no desire for it, no need. I shall never want to smoke again.' I thought that for a few seconds and then went to bed. Next morning I did not even think about smoking, and have never smoked from then until now. By using this method I had destroyed the desire and need for smoking. It is a method, not of supplanting the will but of supplementing it. Indeed, I would go farther and say that it is a form of mind training whereby one reaches a completed will.*

*William Brown, D.M., D.Sc., F.R.C.P.: *Mind, Medicine and Metaphysics*, London, 1936.

Hippocrates*

Hippocrates' COLLECTION contains the following case history: a superb example of terseness of expression and precision of comment:

"In Abdera Pericles was seized with acute fever, continuous and painful; much thirst; nausea; could not retain what he drank. There was slight enlargement of the spleen and heaviness in the head.

First day. Epistaxis (bleeding) from the left nostril; the fever, however, increased greatly. Copious urine, turbid and white. On standing it did not settle.

Second day. General exacerbation (in symptoms); the urine, however, had consistency, but there was some sediment; the nausea was relieved and the patient slept.

Third day. The fever went down; abundance of urine, with concocted and copious sediment; a quiet night.

Fourth day. About mid-day a hot, violent sweating all over; crisis; no relapse."

*Garland, Joseph, M.D.: *The Story of Medicine*.

It is a great misfortune neither to have enough wit to talk well nor enough judgment to be silent. — La Bruyere

*Look round the habitable world; how few
Know their own good; or, knowing it, pursue. — Juvenal*

Triamcinolone Hexacetonide*

Sublesional Use Of

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DESPITE THE LARGE number of steroid products now available, there are relatively few experiments published in the literature concerning their intralesional or sublesional use in the treatment of various dermatologic disorders. This route of administration has several obvious advantages. Compared with oral administration, sublesional injection allows the effective use of steroids in much smaller doses and thus greatly reduces the risk of the well-known systemic side effects of these compounds. When compared with topical applications, sublesional use avoids the variations in the ability of the compound to penetrate the skin and the resultant variability of clinical results. It has also been shown that many skin diseases that do not respond to topical steroids will respond to intracutaneous injections.²

The clinical response attained from the application of steroids to dermatologic lesions depends largely on the local concentration of the drug and the length of time it remains deposited at the site of injection. In the past, best results have been reported from the use of the acetate, diacetate, and tertiary butyl acetate of prednisolone and triamcinolone.

In 1961, J. L. Hollander presented evidence that triamcinolone acetonide tertiary butylacetate (hexacetonide) suspension, when assayed by intra-articular injection in arthritic patients, more than doubled the duration of effective relief in the majority of patients tested.¹

These studies and others led to the experimental use of this compound in dermatologic disorders by injection directly into or

*Aristospan® (triamcinolone hexacetonide) — registered trademark of Lederle Laboratories, a Division of American Cyanamid Company, Pearl River, New York.

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immediately under the lesions. It is the purpose of this communication to report such a trial in 45 patients who had not had previous therapy with similar agents.

Materials and Methods

Patients for this study were selected for the presence of a variety of cutaneous diseases (Table 3). No requirements as to age or sex were stipulated. However, ages ranged from 19 to 75 years, as shown in Table 1. There were 20 males and 25 females in this study.

Dosage was based on the sublesional administration of approximately 2 mg. of triamcinolone hexacetonide per square inch of lesion. In all except one instance only one injection of 1 to 5 mg. was required for each lesion. One patient with lichen chronicus simplex (circumscribed neurodermatitis*) was given a second injection one month after the first. No other treatment was administered during the period of study and patients were observed at weekly intervals for a minimum of one month. The results were evaluated by the following criteria: the response was considered to be "excellent" when there was complete clearing of the lesions, "good" when there was less than total clearing but more than half, and "fair" when there was some improvement but more than half of the lesion remained. The results were noted independently by each of the two investigators.

Sixty-one percent of the evaluations were made in patients treated for only one lesion, 22% had two lesions treated, and 16% had three or more lesions treated. Doses ranged from 1.0 to 5.0 mg. and averaged 2.0 to 2.8 mg. per patient (Table 2).

Results

Clinical Response

Although 45 patients were treated in this

TABLE 1
Age Distribution

Age Range	Number of Patients
11-20	2
21-30	10
31-40	8
41-50	7
51-60	8
61-70	8
71-80	2
Total	45

TABLE 2
Average Dose Per Patient

No. of Lesions Treated Per Patient	No. of Patients	Dose Range	Average Dose Per Patient
1	30	1.0-5.0 mg.	2.2 mg.
2	11	2.0-5.0 mg.	2.8 mg.
3	2	1.5-2.5 mg.	2.0 mg.
4	5	1.5-2.5 mg.	2.0 mg.
5			
6			
7			
8	1	2.5 mg.	2.5 mg.
Total	49		

*See Test Your Word Score Page 687.

TABLE 3
Clinical Response to Triamcinolone Hexacetonide

Diagnosis	Number of Lesions	Clinical Response Number of Lesions					Clinical Response No. of Pt. Evaluations			Number of Patient Evaluations
		Excellent	Good	Fair	No Change	Excellent	Good	Fair	No Change	
Psoriasis vulgaris	48	16	29	3		8	11	2		21
Localized neurodermatitis	12	4	7	1		3	6	1		10
Alopecia areata	15	4	8	3		1	5	1		7
Acne cyst	3		2	1			2	1		3
Synovial cyst	2		1	1			1	1		2
Lichen planus	1		1							1
Chondritis with serositis	2	1	1			1	1			2
Granuloma annulare	1	1				1	1			1
Necrobiosis lipoidica	1				1				1	1
Seborrheic dermatitis	1		1				1			1
Total	86	26	50	9	1	14	28	6	1	49
Percent	100.0%	30.2%	58.1%	10.5%	1.2%	28.6%	57.1%	12.2%	2.0%	100.0%

study, three of the tabulations (Tables 2, 3, and 4) are based on the premise that those patients treated on more than one occasion constituted a separate evaluation of the efficacy of the drug. This situation occurred in three patients, two of whom were each treated on two different dates, and one who was treated on three different dates, making a total of 49 evaluations in 45 patients.

Ten discrete disease entities were diagnosed. Of a total of 49 observations, 14 or 28.5% resulted in an excellent response, 28 or 57.5% were judged good, and seven or 14.3% were fair or without change (Table 3). The majority of patients were treated for psoriasis or localized neurodermatitis. In both of these groups 90% of the evaluations showed excellent or good results. It is interesting to note that all evaluations were made independently by each of the two investigators with a high degree of correlation.

During these 49 patient evaluations, 86 lesions were treated. Table 4 summarizes these clinical responses. In 88.2% of the lesions treated, results were judged to be excellent (30%) or good (58.2%).

Duration of Response

During each patient evaluation the time of onset of effective response and the duration of this response were noted. In those patients with excellent and good responses, the onset of improvement was noted within two weeks of the administration of the drug. When pruritus was present, definite relief occurred frequently within 24 hours of

treatment. There followed a gradual diminution of swelling, erythema, and scaling, and a reduction in the size of the lesion.

In all but three cases, the drug was still effective at the end of the study (for the number of days tabulated in Table 5) and there was no regression of the lesions during this time. In one patient the effects of one injection lasted only two weeks. However, another injection given a month later produced good results that still persisted at the termination of the study two months later. Thirty-four of the 45 patients (75.5%) had effects lasting for 35 days or more.

Side Effects

The observed side effects involved three patients, each of whom developed a sterile abscess, and one in whom there was a hemorrhagic reaction at the site of the injection. All of these subsided uneventfully and did not appear to interfere with the efficacy of the drug. In addition, three instances of mild cutaneous atrophy occurred. One patient developed two of these areas of atrophy which have remained for six months. No systemic reactions were seen.

Discussion

The course of psoriasis, neurodermatitis and other dermatoses is frequently unpredictable. Spontaneous remission or exacerbation is not uncommon. Although controlled studies are usually desirable, it is necessary to assess the disadvantages of various types of controlled studies when evaluating the treatment of these diseases.

Placebo Controls or Untreated Controls

Both psoriasis and neurodermatitis, which constitute the majority of cases treated in this study, are influenced strongly by psychological factors. Thus, in diseases of this nature, a prominent placebo effect, or spontaneous changes in untreated patients, can be predicted.

Paired Comparisons

When treating some lesions in one patient with an active drug and other lesions with a placebo, the results may be undecisive due

TABLE 4
Onset and Duration of Effective Response

Days	Number of Patients	
	Onset of Response	Duration of Response
0-6	7*	2*
7-13	34	7
14-20	8	3
21-27		
28-34		3
35-41		3
42-48		4
49-54		4
55-61		5
62-93		18
Total	49	49

*One patient had no response.

to the effect of systemically absorbed drug on the placebo-treated lesions.

Crossover Treatment with Two Drugs

This study design is complicated by two factors: (a) the possibility of an effect of residual drug on the second phase of the trial, and (b) the lack of a true base line for comparison (e.g., the disease is not in its original, untreated state after the administration of the first course of treatment). In both cases the second phase of the trial is difficult to evaluate because of the existence of a previous course of treatment.

The disadvantages of an uncontrolled study are well known. However, an effort was made to draw valid conclusions by creating objective criteria for the evaluation of the clinical results, and by having these results judged independently by two investigators.

Summary and Conclusions

Forty-five patients were treated for a variety of cutaneous disorders by the sublesional injection of triamcinolone hexacetonide. Within two weeks of treatment, the majority of patients had excellent or good results which lasted for 35 days or longer. With doses limited to approximately 2 mg. per square inch of lesion, local side effects were minimal. Sterile abscess, hemorrhagic reaction, and mild cutaneous atrophy occurred at the site of injection in 1.5% of the patients. These reactions were mild in degree of severity and did not interfere with the efficacy of the drug. All of these local reactions were transient with the exception of the mild cutaneous atrophy which persisted for approximately six months at two sites in one patient. However, these appeared to be slowly subsiding. There were no systemic reactions noted in any patient in this study.

References

1. Hollander, J. L., et al.: A New Intra-Articular Steroid Ester with Longer Effectiveness, presented at Annual Meeting American Rheumatism Assn., New York, June 22, 1961. (Unpublished)
2. Stoughton, R. B.: Steroid Therapy in Skin Disorders, JAMA 170:1311, 1959.

Nature's Insuperability

In the inner cavity of the larynx there is a structure of peculiar formation, which we have already shown to be the principal organ of the voice. It resembles the mouthpiece of a reed-pipe, especially when seen either from above or from below. Instead, however, of comparing the glottis with the tongue of reed instruments, it would be more appropriate to compare them with the glottis. For the works of Nature are both earlier in time, and more perfect in construction, than those of art; and, as the glottis is the work of Nature, while the reed-pipe is the production of art, it is possible that the latter might have been made in imitation of the glottis by some clever artist, able to understand and copy the structure of natural objects. — Galen

In the problems which the Almighty sets his humble servants things hardly ever happen the same way twice over, or, if they seem to do so, there is some variant which stultifies undue generalization. The human mind, except when guided by extraordinary genius, cannot surmount the established conclusions amid which it has been reared.

— Winston Churchill, *The Gathering Storm*

Nobody ever forgets where he buried the hatchet. — Kin Hubbard

No great man ever complains of want of opportunity. — Emerson



Editorials

I Remember. I Remember

*"How dear to this heart are the scenes of my childhood
When fond recollection presents them to view!"*

Samuel Woodworth

IT HAS OFTEN occurred to me that one of the most valuable, yet least recognized natural defense mechanisms of man is the ability of the brain to store away countless memories — good and bad — and after doing so to be able to eliminate from immediate consciousness those recollections which are unpleasant, thus allowing him to dwell upon happy memories of the past. Were it not so, life would be intolerable; we should either become misanthropes or go mad.

World War I

Thus it is that recollections of our youth, despite hardships, assume a roseate hue. In March 1917 the Russian Revolution began and in April the United States entered World War I, a titanic struggle which was to become the greatest military holocaust in history up to that time. But it is easier — and therefore, more pleasant for me to recall that during 1917-18 I was a senior in Medical School at the University of Minnesota, that we students were beginning to see patients and feel a little like physicians, and that our work-load of lectures and classes had suddenly become much lighter. The relief was so great that I was able to scratch a long-standing itch by joining the Masquers and other drama groups on the campus. I had previously taken some courses in Speech

with Dr. Frank Rarig and as a result of these experiences became convinced that every university student, as a potential leader in his work or in his community or in both, should have a substantial amount of training in the art of public speaking.

The Influenza Epidemic

But this welcome extracurricular freedom was not to last long. Some time during 1917 an ominous cloud, aside from but concurrent with the war, appeared in the East. An outbreak of influenza, more insidious and destructive than any epidemic of modern times, began to roll toward the United States from abroad. By late 1918, when it finally began to subside, the disease had killed an estimated twenty million people throughout the world, including 548,000 members of the American Armed Forces.

In June 1918 my medical class graduated and all the men were immediately inducted into military service, receiving the new degree, "Bachelor of Medicine." After passing the State Board examinations it would have been entirely legal for us to practice medicine in Minnesota (although none of us did) as "Mr." rather than "Doctor" Jones, as was the case with many physicians and surgeons in England for a long time.

Some of the graduates joined Base Hos-

Continued



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pital 26 for service in Europe. Arthur Law was head of the surgical section and S. Marx White of the medical division of this unit, these graduates having been given their M.D. degrees before leaving. Others were assigned to duty as internes; of these a number, including myself, went to the then Minneapolis (now Hennepin County) General Hospital and received their M.D. degrees upon completion of their internships in 1919. Among others in the Base Hospital group were E. D. Anderson (Ted became ill after some years in the practice of pediatrics and moved with his family to Switzerland), Egbert Borgeson, Woodard Colby, Harold Diehl, David Kadesky, Elmer Lundquist, Donald McCarthy, Albert M. Snell and Carl Swendseen; in the General Hospital group were Ed Norris, Sam Weisman, Stillman Hathaway, William Peyton, Laurits Ylvisaker, Anderson Hilding, George McGear, Morris Nathanson, C. L. Roholt, et alia.

The General Hospital was literally filled with desperately ill influenza cases. Rooms, wards, halls and corridors were crowded with beds. Despite our best efforts, the death rate, especially from pneumonia, was high.

Armistice Day

During all this time the war was grinding on. In January 1918, President Wilson made his celebrated 14-Point address to Congress, calling among other things for the self-determination of nations, the removal of economic barriers and the establishment of a League of Nations. In July 1918, Czar Nicholas and his family were assassinated. Finally, on November 11, 1918, the Armistice was signed and World War I ended. What a day to remember!

Unmarried Interns

Once again, with the war over, and the epidemic subsiding, we could begin to relax. Many of us had struggled so hard to put ourselves through Medical School, financially and scholastically, that we had had time for almost nothing else but work. Now, suddenly we discovered girls — pretty, bright nurses in their crisp blue and white uniforms. But there was one great obstacle: student nurses were forbidden to have social

contact with members of the attending or interne staff, except at occasional dances in the Nurses' Home. So what could be more natural than that nurses and internes meet elsewhere; if some of us internes were a little awkward and lacked skill, the girls didn't seem to mind. It must be remembered that in those days there were practically no married student nurses and very few married internes.

Well, meet they did, and as a result many romances and marriages developed. A few come to mind: Verne Walsh and Larry Doyle; Veda Newman and Nels Gunderson; Ruth Daly and Frank Hirshfield; Blanche Rucker and Hillard Holm; Ann Dahl and Joe Neal; Mary Dean and Virgil Schwartz.

In 1917, and for some years before and after, there were staff problems at the General Hospital. There were two services in almost every department: the A service was staffed by men with University affiliation, the B service by men without University connection. If memory serves me well, the head of A medicine was Henry Ulrich, the head of B medicine, Soren P. Rees. The head of A surgery was Arthur Mann, the head of B surgery, A. E. Booth. Most other departments had similar dichotomous arrangements. A good deal of disharmony was thus engendered and continued for years until a sort of detente developed, leading eventually to assumption by the University of all teaching responsibility for internes, medical clerks and students. This produced one of the finest clinical teaching facilities in Mid-America.

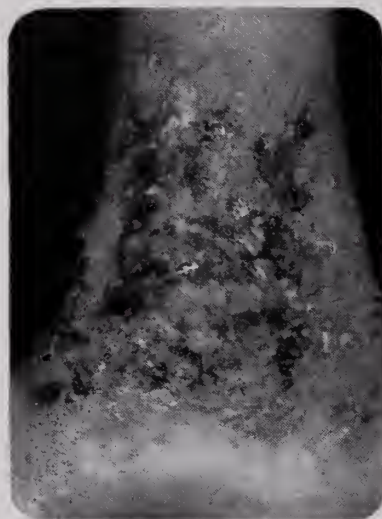
Antibiotic Era

Great changes have taken place in medical thought and action since 1917. One of the most powerful forces in modern history, antibiotics, was only a word in the unabridged dictionary. Many of the other medical tools and ideas which we now employ daily were unknown then. The now rapidly expanding fields of ecology,* cybernetics and others with their probable medical implications were also not known or understood.

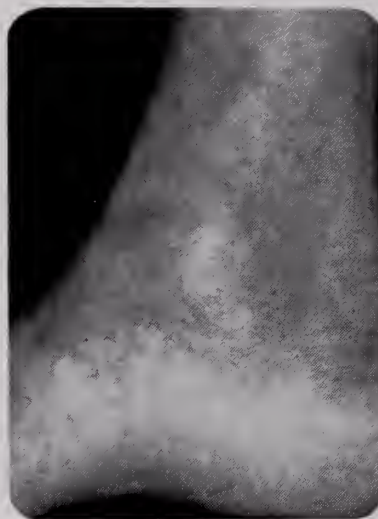
And how some ideas and value judgments

*See Test Your Word Score Page 687.

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have changed! Random opening of the 1917 Volume of "The Journal Lancet" discloses an editorial (Page 120) which states in part:

Planned Parenthood

"A pamphlet entitled 'Family Limitations' by Margaret H. Sanger is the pamphlet that has caused so much discussion relative to birth control; . . . the newspapers have detailed the account of Mrs. Sanger's arrest, and her imprisonment for thirty days for circulation of the pamphlet, as well as for clinics that she conducted in New York and Brooklyn. The pamphlet is by far one of the plainest and broadest that has ever been circulated. . . . A few years ago a physician of Minneapolis wrote a book on sexual problems dealing with birth control. His book was confiscated, he was arrested, tried for dissemination of obscene literature, and *was sentenced to the penitentiary for one year*. Mrs. Sanger, however, gets off with thirty days, which is too short a sentence considering the advice that she gives women in her clinics and through her pamphlet."

The Golden Years

The gentlemen whom we honor in 1967 upon the completion of fifty years of medical service to the people of Minnesota have seen all of the preceding changes and many more. In addition to the eradication of countless infections by means of antibiotics, they have witnessed vast improvement in the management of diabetes and tuberculosis, the control of pernicious anemia, the virtual elimination of smallpox, rabies, diphtheria and poliomyelitis. They have seen spectacular achievements in the field of thoracic surgery, both pulmonary and cardiac, beginning with the removal of a lung by Evarts Graham in St. Louis, on through the expanding area of neurosurgery and up to the present work in organ transplantation. There is still much to learn about the cause and cure of cancer, aside from early diagnosis and treatment, and about heart and cerebrovascular disease, genetic problems, degenerative diseases of old age, and many others; but we can hope

that the sons and daughters of these fine men will help in accomplishing these monumental tasks.

Of the twelve physicians whom we honor this year, I have heard glowing reports, both personally and professionally. They are Einar Andreassen, John Stuhr, Fritz Pearson, Gustaf Nordin and Herbert Molander. Andy Sinamark is an old and valued friend; his work in the fields of ophthalmology and otolaryngology in Hibbing is known and appreciated throughout Minnesota. In addition, he has contributed valuable time and effort to a non-profit, voluntary organization, The Minnesota Society for the Prevention of Blindness. Ed Robb practiced pediatrics on a high level, with Drs. Rodda, Wilder and others for many years in Minneapolis. Art McFarland is a dear old friend who seems just as active and alert today as he was when he first joined Dr. Louis Nipert in practice years ago. He is the only medical man I know who was so conscientious, sympathetic and successful in his work that a wealthy patient made him a present of an expensive automobile; Tom Devereaux keeps rolling along in Wayzata; the years do not seem to affect him either. He and Dr. McFarland and I have been members of the Eitel Hospital staff for many years. John Lepak finished his teaching fellowship at the University Hospital a year or two before I began mine; his outstanding reputation in the field of internal medicine is well known. Charles Conner was a careful, able otolaryngologist whose office was adjacent to that of ophthalmologist Frank Burch. Ted Sweetser has been an outstanding urologist in Minneapolis for years. He and I enjoyed the dubious pleasure of being retired from the University faculty on the same day a few years ago.

It has been a rich experience to have had the friendship and the opportunity to emulate the qualities of these admirable men. We wish them all many more years of good health and fruitful endeavor.

Virgil J. Schwartz, M.D.
Minneapolis, Minnesota

Fame is something which must be won; honor is something which must not be lost.
—Schopenhauer

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The Disturbed Patient

IF AN AMERICAN Board is established in the Art of Medicine, the practical examination will be given on the type of cases described by Babb and Steinhilber elsewhere in this issue.* For a physician mastery of the art of handling patients (the Art of Medicine) is a prerequisite to successful therapy. It is difficult for the physician in training, concentrating his entire attention upon anatomic and physiologic evidence of disease, to devote equal attention or even any attention to the emotional problems which may be of significant importance. The fundamental purpose of visiting the patient must be to prolong life and relieve symptoms. Sometimes this may be done by discovering an elusive physical finding leading to the diagnosis of an unusual disease, followed by medical or surgical cure, a very satisfying outcome to the patient and especially to the physician.

When a vast and expensive medical survey leads apparently to nothing, the physician may be as frustrated as the patient. Under such circumstances the physician may react ineptly, artlessly, in response to his own frustration, fixing a label of hysteria or neurosis on a patient because the studies de-

signed to discover the disease turn up all blanks.

The greatest rewards in medicine should be in the proper care of the neurotic, hysterical, and psychotic patients. There is no great art to the successful diagnosis and treatment of a straightforward medical problem in a patient able to give an accurate history, who accepts reasonable diagnostic procedures, and follows therapeutic instructions carefully. The real expression of the art of medicine is exemplified in the physician's care of the difficult patient who cannot give a logical history, who has symptoms in every system, and discourses at length upon the difficulties he has with each and every one of his organs. It is satisfying to pluck the plum of pathology from the foliage of noncontributory symptoms. It is less satisfying but equally important to handle the situation when no such pearl of disease appears. Should this prove to be an excessively frustrating experience to a young physician, he should consider avoiding general practice and internal medicine, where this situation is the rule rather than the exception. There is, however, great satisfaction for the physician skillful in the art of the care and feeding of the neurotic patient.

Reuben Berman, M.D.
Minneapolis, Minnesota

*See page 649.

The object of any piece of writing is to make your reader understand exactly what you have to say — and understand it as quickly and effectively as possible. To make your reader do this you must lay out your article, report, story — whatever it may be — like a carefully surveyed road. Otherwise it will never get anywhere in particular; it will merely stop short after a certain number of pages. For lack of plan too many pieces of writing find themselves “miserably straggling to an end in sandy deltas.” We are all too busy to read that sort of thing.

David Lambuth
The Golden Book on Writing

Most medical fads are like some women's fashions — frail, fickle and costly.
— Noah Fabricant



She simply sits while the party goes on around her, already used to being the girl who is left out. She tries to lose weight—but her emotions won't let her. She becomes irritable and depressed when she doesn't eat, and anxious when she considers her future. So each time she gives up.

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Observations on the Diagnostic Capabilities of Laboratory Tests

A RECENT ARTICLE* in MINNESOTA MEDICINE describes an attempt to evaluate the diagnostic value of decreased serum cholesterol levels — an attempt of special interest in that it considers the influence of the presence of pathological states *other* than the one for which the test is requested. Thus it seems timely to consider some general questions concerning the informational value of laboratory tests in medical practice.

The clinician has come to rely heavily on the laboratory to assist in providing information on which to base a diagnosis. However, the diagnostic implications of test results are frequently not clear. Hence, an evaluation of the diagnostic capabilities of tests is essential.

Diagnosability

One of the most important considerations in determining the value of a test is the probability (or odds) that a person has the disease if the test result is "positive." For this probability we shall employ the term "diagnosability of the test."** Before exploring the concept of diagnosability, we must consider two other properties of tests. First, not all persons with a disease yield a positive test result. *Sensitivity* is defined as the probability that a person with the disease *will* have a positive test (i.e., the proportion of people with the disease who will yield a positive test). Thus, if the test under consideration has a sensitivity of 93%, a person with the disease has a 93% probability of yielding a positive test. In contrast, 7% of those with the disease will yield a negative test. These 7% are called *false negatives*.

Second, *specificity* of the test is defined as the probability that a person free of the disease will yield a *negative* test. Thus, if a test has a specificity of 96%, a person free of the disease has a 96% probability of yielding a negative test. However, 4% of those without the disease will yield a positive test.

These 4% are called *false positives*.

Now, again consider diagnosability and its formulation. Postulate, for example, a test with:

1. a sensitivity of 95% and
2. a specificity of 95%

(this test would generally be regarded as a good one indeed).

Consider further, as an example, a population of one million persons, 1000 of whom have the disease (a fact usually estimable from experience, e.g. from surveys). Thus, the *prevalence rate* of the disease is 1 per 1,000. The formulation begins with the following table:

TABLE 1

Total Population	Diseased	Not Diseased
1,000,000	1,000	999,000

Since the sensitivity of the test is 95%, 950 of the 1,000 diseased persons will demonstrate a positive test result and 50 a negative test:

TABLE 2

Total Diseased	Test Positive	Test Negative
1,000	950	50

Since the specificity of the test is 95%, then 95% of the 999,000 individuals who are not diseased will demonstrate a negative result and 5% a positive test:

TABLE 3

Total Not Diseased	Test Positive	Test Negative
999,000	49,950	949,050

The preceding two tables illustrate that the hypothetical population would have 50 false negatives and 49,950 false positives if all million individuals were tested. The three tables can be combined into a single table which leads to the additional information needed to arrive at diagnosability:

Table 1 appears as the lowest line of Table 4. Table 2 appears as the left hand

Continued

*Hunter, Dewitt T., Hypocholesterolemia, Minnesota Med 49:1555, 1966.

**Since the authors of this editorial coined this term and considered its formulation, it has come to their attention that a similar concept has been described by Thomas J. Vecchio, M.D., in the New Engl J Med 274:1171, 1966.



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TABLE 4

Test Result	Diseased		Total
	Yes	No	
Positive	950	49,950	50,900
Negative	50	949,050	949,100
Total	1,000	999,000	1,000,000

column of figures of Table 4, and Table 3 appears as the middle column of figures of Table 4. The right-hand column of Table 4, Total Positive and Total Negative, is new information. Now the diagnosability is defined as the proportion of those with a positive test who turn out to have the disease. In this example the diagnosability would be equal to 950 (those with the disease and with a positive test) divided by 50,900 (those with a positive test with or without the presence of disease). If one pursues the arithmetic, he will find that the diagnosability of this hypothetical test *in this situation* is 0.019 or 1.9%! In other words, a person with a positive test has less than a 2% chance of having the disease, and this using a test with 95% sensitivity and 95% specificity (a good test)!

With a little algebra the following formula can be shown to hold where D = diagnosability, S_e = sensitivity, S_p = specificity, and P = prevalence rate of the disease:

$$D = \frac{(P) (S_e)}{(P) (S_e) + (1-P) (1-S_p)}$$

A few comments are in order concerning the characteristics of this formula (besides the fact that a good test can yield a disappointing diagnosability):

1. The diagnosability improves with higher sensitivity and/or specificity, everything else being equal. (The results in the example would have been even poorer with a sensitivity and/or specificity less than 95%).

2. The diagnosability would be 100% if the specificity were 100%, no matter what the other variables were. A similar relationship *does not* hold with respect to sensitivity.

3. *The diagnosability depends very strongly on the prevalence of the disease in*

the population. For example, with a test of 95% sensitivity and 95% specificity and with a prevalence rate of 50% (i.e., half of the population has the disease), the diagnosability would be 95%. Thus, *diagnosability is not a static, constant factor but varies according to the situation in which the test is applied.*

It is essential, at this point, to enumerate some of the assumptions in the use of the above formula:

1. We are dealing with a definable illness condition.

2. We have a test which can be categorized as positive or negative.

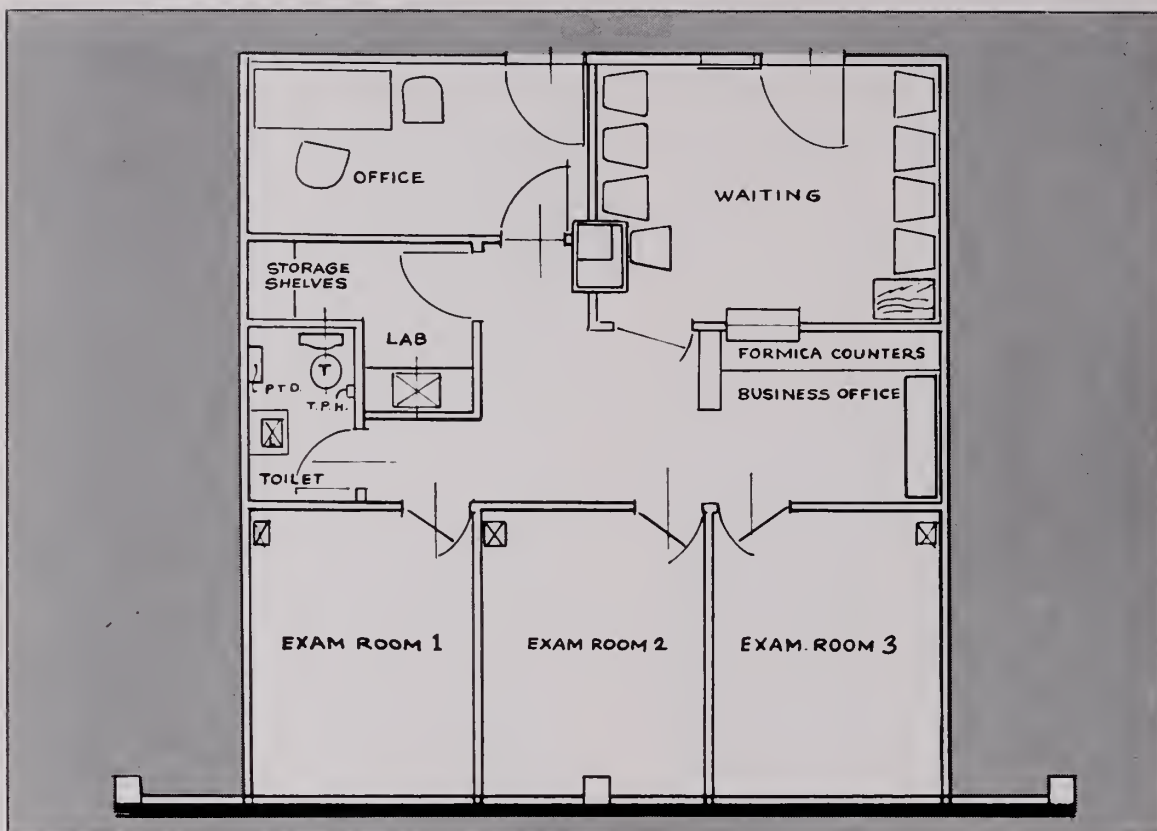
3. We know (from experience, possibly from a survey) the sensitivity and specificity of the test and the prevalence of the disease.

We frequently do not know the answers to some of these implied questions. We can sometimes get approximations, via other means, to the variables listed in 3. And we have to modify our conclusions as assumptions 1 and 2 are not met.

End-Point or Disease State

One of the important problems concerns the definition of the end-point or disease state. Are we dealing with a well-defined single pathologic condition, a group of illnesses, or a vague state of illness? What happens when a person also has another illness which may affect the test result one way or another? (This is the root of the problem considered by Dr. Hunter.) In the present example, the situation is such as might be encountered in mass screening where no information is available about the subject other than the test result. But when the clinician orders a test performed, he orders it because he has a suspicion based on other information he has about the patient. Thus, a person with a positive result to the test described in the example may have a greater than 2% chance of having the disease if he also has certain signs and symptoms. One satisfactory way around this problem might be to consider the *conditional* use of the formula. The sensitivity of the test might be higher for persons with more

Continued



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severe illness who have signs and/or symptoms that cause them to seek medical attention. And, more important, the prevalence of the disease may well be higher among those who have certain signs and symptoms than among the general population. Whether or not other diseases will have an effect on test results would influence the sensitivity and specificity of the test for the disease under consideration. Hence we should perhaps employ the formula separately and derive separate estimates of diagnosability, *given different sets of other information about groups of subjects*. Such separate estimates are called *conditional* probabilities, in technical statistical jargon.

Philosophical Problems

There are many philosophical problems involved in diagnosis in general, as well as in interpretation of laboratory results. For instance, what is the definition of an illness? Is it based on microscopic pathologic status (e.g., astrocytoma of the brain) with the symptoms described only as associated with the illness? Is it based on physiologic aber-

rations (e.g., right heart failure)? Is the test result itself considered a diagnosis (e.g., hypocholesterolemia)? What is a "positive" test or what should it be? Is the test used singly or in combination with other tests? These and many other problems (e.g., laboratory errors and refinement of test mechanics) are important to the subject but are beyond the scope of this communication.

Thus, while the arguments presented above can not provide complete or definitive answers to the problems of test interpretation (nor could they in such a brief and general treatise), it is hoped that the reader may gain some additional insight into rational criteria for interpretation of test results. One thing is certain: while laboratory tests can be very helpful in diagnosis, they cannot supplant clinical judgment based on *all* of the relevant and available information. Nor will it ever, in our opinion, be possible to use any formula as a replacement for clinical acumen, but rather only as another tool in the physician's diagnostic armamentarium.

*Division of Epidemiology, School of Public Health, University of Minnesota.

**Division of Biometry, School of Public Health, University of Minnesota.

Warren H. Gullen, M.D., M.P.H.*
Jacob E. Bearman, Ph.D.**
Minneapolis, Minnesota

Radical Pancreatoduodenectomy: Diminishing Mortality Rate

THIS REVIEWER was taken to task several years ago by a purist in the profession for having spoken of tumors of the ampulla of Vater. It was pointed out that an ampulla is merely a dilatation or opening and that, properly speaking, we should always use the term papilla of Vater. This seemed a minor point to me, but I suppose we should all correct our habits.

The article of Dr. Yoshio Sako* presents quite lucidly the experience of one group of physicians with tumors which are most difficult to cure and frequently most difficult to recognize. Their experience has been quite similar to ours, especially in a progressively diminishing mortality rate after

radical pancreatoduodenectomy.

The current efforts directed toward preventing pancreatic fistula after this operation have been largely responsible for the improved rate. The use of an indwelling tube (usually made of a plastic material) within the main pancreatic duct, which is anchored securely and allowed to pass spontaneously later, has been most helpful in our hands. Accurate mucosa-to-mucosa suturing of the duct to the jejunum is theoretically ideal, but it does not provide for the pancreatic juice which might drain from the cut surface of the gland and from tiny ducts which cannot be recognized. For this reason we have continued to invaginate the entire cut end of the pancreas well within the jejunum.

*Sako, Yoshio: Carcinoma of the Pancreas and the Ampulla of Vater. *Minnesota Med* 50:169, 1967.

Continued

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The point is brought out that persistence in resection in too high a percentage of cases leads to poor results because malignancy must be left behind, malignant planes are invaded, and the results are worse than those after mere palliative surgery. Our experience has been that palliation is better after resection than after some lesser operation, because pain is much less of a factor and occlusion of palliative anastomoses may not be so common.

The head of the pancreas continues to be the most troublesome area for the surgeon,

because a tumor there may be much more extensive and invasive than the surgeon originally realized. Until something better is available, we must continue with radical pancreatoduodenectomy, even in cases of malignancy of the head of the pancreas, because we are seeing an increasing number of five-year survivals. At the same time we must be alert to all possible contraindications so that we will not be attempting the impossible.

Edward S. Judd, M.D.
Rochester, Minnesota

Test Your Word Score

Neurilemmomas — *a tumor of the peripheral nerve sheath* (page 638).

Organoid — *resembling an organ* (page 640).

Pellitory of the wall — *a plant resembling yarrow, the root of which is used as a sialogue (to promote the flow of saliva)* (page 648).

Catecholamines — *such as adrenaline and noradrenaline* (page 654).

Hemianopsia — *loss of vision in half the visual field* (page 659).

Treponema pallidum — *the causative agent of syphilis in man* (page 665).

Neurodermatitis — *dermatitis of emotional origin* (page 670).

Dichroic — *presenting one color in reflected light and another in transmitted light* (page 666).

Ecology — *dealing with mutual relations of organisms and their environment* (page 675).

Rhabdomyosarcoma — *a combined sarcoma and rhabdomyoma (a myoma composed of striated muscular fibers)* page 710).

Huntington's Chorea — *hereditary chorea* (page 717).

Kyphoscoliotic — *characterized by backward and lateral curvature of the spine* (page 737).

Artefact — *any tissue that has been mechanically altered from its natural state* (page 753).

Cryoprecipitated — *precipitated by freezing* (page 778).

Derivatively Speaking

Why are the five vertebrae between the lumbar and the caudal called the sacral? — Because they constituted the preferred portion of the animal victim offered up as a sacrifice in early religious rites. Hence it became sacred and was called the sacrum.



look, kid, I gotta know your birthdate

Age *is* important because many coverages are in force by age
(we like to know for utilization studies, too). If your office does
not have the exact date, we must at least know the month
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BLUE SHIELD
OF MINNESOTA



You May Be Right

An Obstetrician Proposes a Change in the Abortion Laws

The recent controversy over the proposed changes in the state abortion law have been directed primarily to the change recommended by the American Law Institute in 1959. Those in favor of such a change point to the three major areas where legalized therapeutic abortion is needed, namely, rape, incest, and for medical (organic or psychiatric) disease of either the mother or fetus. The opposition to this change is concerned with the eventual outcome after physicians are given broad license to interrupt pregnancy.

To the practicing physician the theoretical problem is neither moral nor medical. It is the repugnant fact that currently antiquated legal statutes dictate how a scientific judgment must be made. Although the theoretical punitive threat probably does not alter many decisions, the performance of justified abortions outside of the legal sanctions is contrary to intellectual honesty. The principle should be that medical decisions are based upon scientific facts which educated practitioners may agree upon. Thus, if a case arose one should have the legal right to debate the application of therapeutic abortion on scientific grounds alone.

Therefore, it would seem that some compromise law should be passed which would cover the three major areas in question (rape, incest, and medical disease), but which would also offer the protection of sound scientific judgment. The following proposals for incorporation would seem to fulfill this need.

First, in the area of *rape* the obvious problem is the establishment that rape actually occurred and not merely a "change of heart." The new knowledge of reproductive physiology can eliminate this grave decision from the physician's shoulders. We as physicians are now able to effectively prevent pregnancy up to 48 hours *after* intercourse. This has been demonstrated by Morris and Van Wegenen.¹ In the true rape case the victim would only have to present herself to a physician within 48 hours after the incident and receive the necessary medication. Naturally police, physicians, and the public would have to be educated to this new form of therapy. The fact remains that therapeutic abortion is *not* needed as a solution to this problem.

The second area of concern is that of *incest*. Again, the establishment of this social crime is difficult and could best be made by our legal colleagues. I would therefore suggest that the "crime" must be decided upon by a judicial hearing. If it is established to be an incestual pregnancy, the law should allow for therapeutic abortion if the concerned parties so desire. This would also provide for the prevention of a recurrence of this act since the judicial establishment of the incestuous act would automatically lead to prosecution of the actor.

Finally, the much broader area of *medical* indications is changing continually. It is not my purpose to debate specific medical indications such as nephritis, heart disease, depression, rubella or the ingestion of

Continued



Blessed event?

Not entirely, when nausea and vomiting occur in early pregnancy.

Emetrol offers prompt and safe relief. Local rather than systemic action provides emesis control on contact with the hyperactive G.I. tract.* In a study of 123 pregnant women, the drug produced measurable improvement in 79% of patients in controlling vomiting.¹

*As shown by *in vitro* studies.

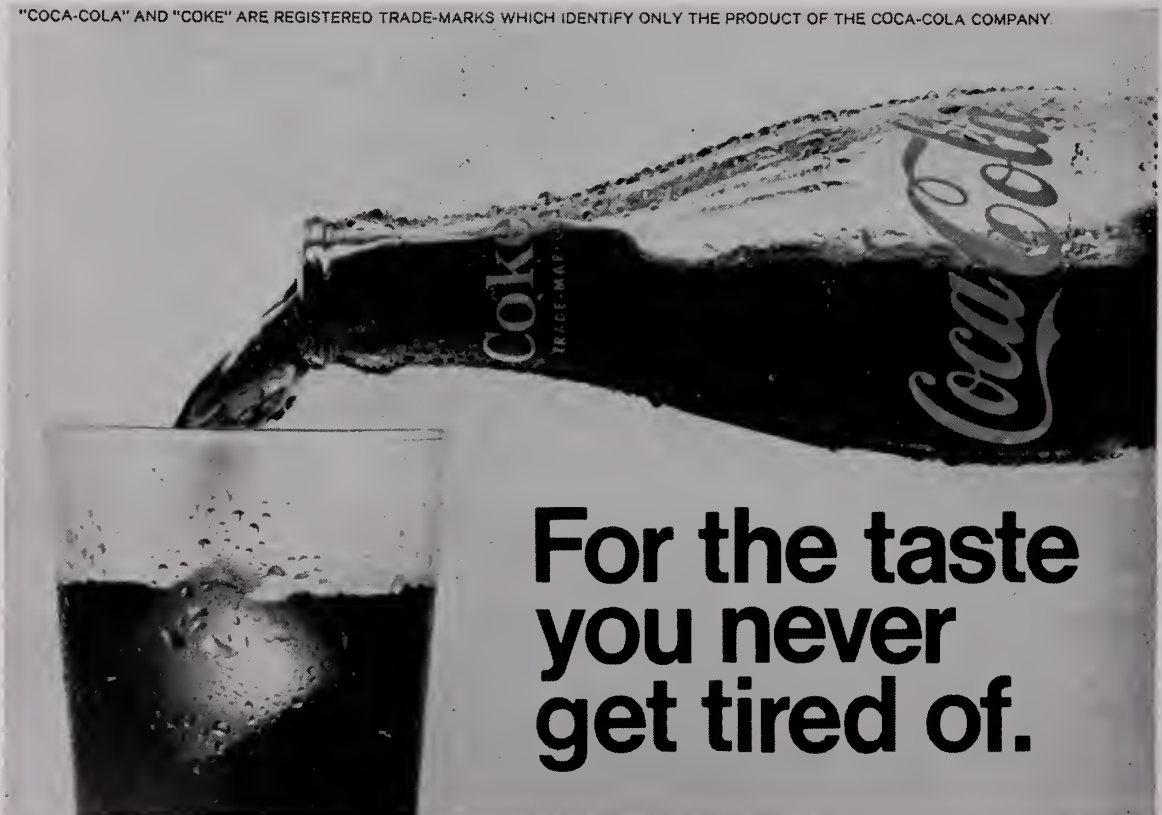
1. Crunden, A. B., Jr., and Davis, W. A.: Am. J. Obst. & Gynec. 65:311 (Feb.) 1953.



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solution
emesis control

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drugs like thalidomide. I believe that when the dangers of a medical problem are established physicians can agree upon the correct action. If the medical effects are uncertain there will be disagreement. Few physicians would argue with the therapeutic axioms of insulin treatment for diabetic patients with acidosis or penicillin treatment for patients with beta hemolytic streptococcal pharyngitis. These areas seem clear. To provide the safeguards to ensure that scientific facts are determining the abortion recommendations, therefore, I would propose that the decision be made by a majority vote at a committee meeting. The committee should be composed of five physicians not including the aborter. Members of this committee should include one board-certified obstetrician, one internist, one pediatrician and one psychiatrist. If anyone objects to this form of committee decision on the basis that it is difficult to establish it in the small community, then I would suggest that the consideration of destroying a human life is the greatest decision that a physician will ever make and merits patient transfer to a center where this group of experts could be assembled. Whether or not a specific medical indication is valid will depend upon scientific judgement. This would also offer the patient expert medical consultation to be certain that other less well known forms of therapy were not being overlooked. Regardless of one's moral convictions, if a group of knowledgeable scientists recommended a form of therapy, this should be acceptable if one is not required to perform the act himself. Finally, the performance of therapeutic abortion should be a reportable operation under state law and this would then allow an analysis of data and a control over committee decisions.

The broad principles for a new abortion law have been presented. The pros and cons of the individual "trees" have not been debated but only the concept of the "forests." This then would represent a compromise which would legally allow for the performance of therapeutic abortions, but would also supply safeguards to guarantee that abortion would be performed only for sound scientific reasons. The technical wording of such a law has not been presented since it would seem more logical to have this done by those who are so trained. It is hoped that such wording would be guided by sound medical judgment.

William N. Spellacy, M.D.
Minneapolis, Minnesota

Reference

1. Morris, J. M., and Van Wagenen, G.: Compounds Interfering with Implantation and Development. III. The Role of Estrogens. *Am J Obstet Gynec* 96:804, 1966.

Perspective

I look through a half opened door into the future, full of interest, intriguing beyond my power to describe, but with a full understanding that it is for each generation to solve its own problems and that no man has the wisdom to guide or control the next generation. — William Mayo

Fashions in therapy may have some justification; fashions in diagnosis have none.
—Herrick and Tyson

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The Editor's Soliloquy

Your Senior Peers

By public consensus I have finally become a 'senior citizen.' I deplore the term — not because of the chronological age it signifies but because of its sly innuendoes. As the word 'juvenile' implies callowness and lingering moisture behind the ears, 'senior citizen' (while sounding smugly dignified) is no more than a genteel substitute for 'oldster' — connoting peering eyes, cupped ears, unlatched jaws, a Parkinsonian hand, doddering locomotion, failing comprehension, and all the rest of the dreary reminders that mortal man's path leads but to the grave.

However, infirmity does not arbitrarily set in the very day a man becomes 65. It can be evident long before that date; it can delay until long after; happily it may never make its appearance.

Some Eastern societies revere their elderly members; some even worship their ancestors. In our culture, however, when we defer to our seniors, it is all too often in a veiled tone of patronage instead of with genuine respect.

If 'junior' would only list when his elders suggest: "Take thou our best and improve upon it: profit from your heritage — do not repudiate it," then our world would not have to be eternally gyrating in concentric circles through the same point but could spiral upward to even higher levels.

Disavowing all charges of wishful thinking, I prefer to regard the majority of my contemporaries as men seasoned by their years — with undiminished physical vigor and mental capacity attesting to the fact that age need not impair human faculties. I observe these gentlemen walking among us with cool detachment — no longer harried by ungovernable impulses, victimized by undue excesses, or driven by vaunting ambition.

It is with this elite group of so-called senior citizens that I now identify. To our younger colleagues we say: we have not become either pedants or fossils: in essence we are still your peers; but in addition we are the unique possessors of an *esprit-de-corps* acquired by surviving and transcending the hurly-burly of youth and middle age with its caterwauling over mere trifles and agonizing over transient problems that only waste man's precious time and substance.

Finally we say to our junior brotherhood: when you become members of our distinguished 65-and-over fraternity you too can join Robert Browning's Rabbi Ben Ezra in saying:

"Grow old along with me!

The best is yet to be,

The last of life, for which the first was made."

Carl O. Rice, M.D.

Some individuals resemble rare wines; they are in their prime when they are aged.

— C. O. R.

Old Doc Hess says: I can never see much sense in having that warning sign on the back of the car. By the time you see it the danger is over: student driver.

The MINNESOTA MEDICINE



HONOR CERTIFICATE 1967

Manuscript

Demonstration of Tuberculosis in the Human Bone Marrow — Improved Technique

Authors

Emil M. Schleicher, Ph.D. February
Minneapolis, Minnesota

1966
Issue

Minnesota Medicine is honored to have this opportunity to acknowledge the work of its distinguished authors and to express to them applause, thanks and cordial best wishes.

Board of Editors

MINNESOTA MEDICINE



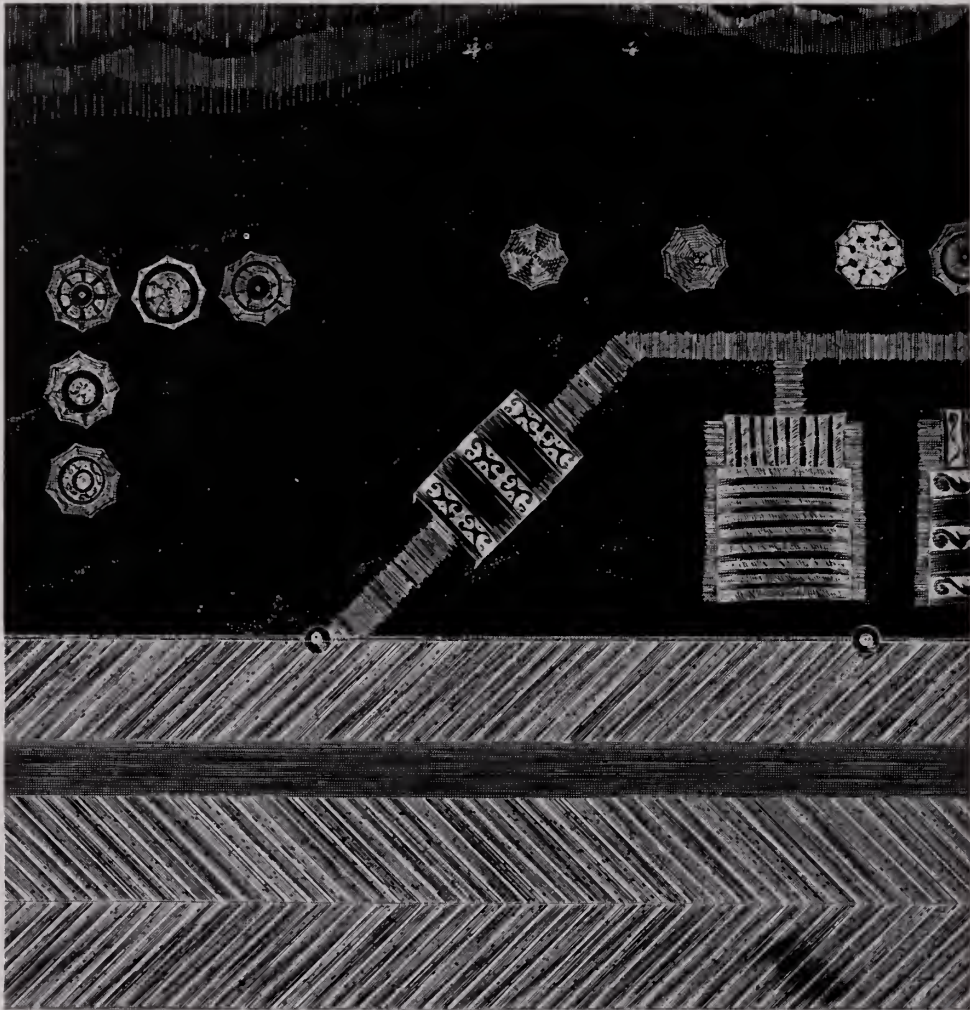
HONOR AWARD

Minnesota Medicine Medical Writing Awards, 1967

It is the pleasure of the Board of Editors to announce the winners of the sixth annual Minnesota Medicine Medical Writing Awards chosen from articles published in MINNESOTA MEDICINE during the year of 1966.

The first place plaque is to be awarded to Doctors Richard L. Reece and Philip A. Olson of Minneapolis. Their article "Coumarin-Induced Bleeding Complications — Report of Eight Unusual Cases from One Hospital" appeared in the November issue of MINNESOTA MEDICINE, page 1677. The presentation will take place during the annual meeting of the Minnesota State Medical Association in Duluth at the New Members, County Officers and Delegates Dinner on Sunday, May 14.

Certificates for excellence in medical writing will be awarded to the author whose article was felt to be particularly outstanding by the Board of Editors.



AMA • 116th Annual Convention • Atlantic City, New Jersey • June 18-22, 1967

Come to Atlantic City—one of America's favorite by-the-sea playgrounds—and join your colleagues at the AMA's 116th ANNUAL CONVENTION!

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RESERVE NOW for the SCIENTIFIC AWARDS DINNER in honor of the Scientific Award Winners—Wednesday, June 21, 1967. Since space is limited, we suggest you make your reservations before June 1, 1967. Tickets are \$10.00 each, payable in advance.

See JAMA May 8, 1967 for complete scientific program—forms for advance registration and hotel accommodations.

Fifty Years of Honorable Service in Minnesota

The presentation of certificates and pins to Minnesota physicians who have engaged in the practice of medicine for 50 years has become an impressive highlight of each Annual Meeting. According to custom the presentations are made during the course of the Annual Banquet. Few who have witnessed these ceremonies soon forget the setting of such an occasion at which these colleagues with a half century of medical practice to their credit so alertly respond to the roll call.

The custom of honoring Minnesota physicians who have served their patients and communities for a half century was established in 1942. Forty-one physicians were honored at the first ceremony. This group also included those who had passed the 50-year mark prior to 1942.

To be eligible for this award a doctor must have spent the majority of his 50 years practicing medicine in Minnesota.

In 1967 thirteen doctors were added to the membership rolls of the Fifty Year Club.

FIFTY YEARS

During the past 50 years filled with interesting and gratifying experiences, I have participated in two world wars, spent six years as a medical missionary in China, 14 years in private practice, and 12 years as the Area Medical Director in the Veterans Administration.

I remember the little Chinese boy with kala-azar, whose enlarged spleen filled two-thirds of his abdomen.

I recall the 300 Chinese wounded soldiers left in a freight train with no one to take care of them except four American boys, Dr. Paul Hodges and me.

I also remember handling other groups of wounded in another war, as the first casualties were returned from the Normandy beaches. Colored men of the sanitary companies handled them so smoothly and gently as they moved them from the L.S.T. boats to the waiting ambulances.

I remember the hospital train and the airfields overseas where the wounded soldiers had to be handled, and I think of the emotions experienced on V-E night in London when the lights were turned on for the first time after several years of blackout.

I remember driving a jeep to St. Lo on the day on which General Patton's army started a wide swing across the Brittany Peninsula. Twenty years later I returned to the United States cemetery at Omaha Beach. All of these incidents and many more come to mind as I think back over the events of the past 50 years.



Einar C. Andreassen, M.D.

I was born at Camelton, Indiana in 1888 and received an A.B. degree from the University of Indiana in 1910 and an A.M. degree in physiology in 1912. I graduated from Johns Hopkins University with an M.D. degree in 1914. Thereafter I served a rotating internship at Rhode Island General Hospital in Providence and a Fellowship in Otolaryngology at the University of Minnesota in 1917.

I served in the First World War in the American Expeditionary Force in France with Base Hospital 88 through the years 1917 to 1919, and did graduate work in otolaryngology at the Universities of Chicago, Pennsylvania, Harvard and Vienna.

I was associated with Frank E. Burch, M.D., St. Paul, in 1919, and I have practiced otolaryngology since then, in addition to being an attending physician at the Wilder Dispensary and the Miller Hospital.

I have been a member of the usual medical societies and began my retirement in 1956.



Charles E. Connor, M.D.

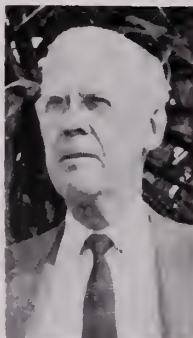
While reminiscing, I recall a beautiful day in June a few years back on the occasion of being a guest at an appreciation dinner given to me by my patients. Mail had been heavy for a few days — with best wishes directed to "Dear Old Doc," "The Old Pill-Pusher" and various other names that I cannot in propriety mention.

As I entered the banquet room I was completely overwhelmed by a group of doctors and their cheerful greeting as we were attended by numerous teenage girls, all of whom I had delivered. They had volunteered to serve as waitresses for a mass of friends and patients ranging in age from 14 to 90.

Warren, who always chided me that my medicine was no good, was there and advised me that he was coming to my office as often as he wished, whether I wanted him or not.

Pat, 85, who was caught by the police driving down the railroad tracks, was also there. He reminded me that I had given him permission to drive. Needless to say, the cops paid me a visit.

Reaching my 50th year in medicine has added a golden leaf to my garden of memories.



Thomas J. Devereaux, M.D.

FIFTY YEARS

A farm in Gnesen Township fourteen miles north of Duluth was my birth place in 1887. After attending St. John's University, Collegeville, and the University of Minnesota, I entered the Medical School and received my Doctor of Medicine degree in 1917.

1919 was the big year during which I opened up my office in the Lowry Medical Arts Building in St. Paul but continued as assistant Professor of Medicine giving clinics at the City and County Hospital in St. Paul. This hospital later became known as Ancker Hospital.

I have been pleased to serve as President of Ancker, St. Luke's and St. Joseph's Medical Staffs. Also many memories are with me from when I served as President of the Ramsey County Medical Society, St. Paul Society of Internal Medicine, Minnesota Society of Internal Medicine, Minnesota Academy of Medicine and Local Chairman of the American College of Physicians.

Cecilia Rosenthal and I were married in 1920, and we have three sons of whom we are very proud. One of our sons is Reverend Roy Conrad at St. Thomas College in St Paul.



John A. Lepak, M.D.

I was born in 1891 in the shadows of Longfellow School in Minneapolis and after attending the Columbia College of Physicians and Surgeons, I interned two years in the New York City Hospital. I was fortunate to be licensed in both New York and Minnesota and practiced with Dr. Harry Harlow Brooks in New York City for one year before entering the army in 1918.

Lillian E. Ferguson of Huntington, West Virginia became my wife that same year, and we have a son and daughter out of this partnership, living in Minneapolis. Besides my gardening and wild life studies, Lillian and I enjoy our six grandchildren.



Arthur H. McFarland, M.D.

Reaching the 50th year in the practice of medicine is an achievement for which I am exceedingly grateful. I give thanks to God, My Heavenly Father, and to Jesus Christ, My Lord and Savior, and the Holy Spirit, my constant companion, who made this a reality in my life.

The east side of St. Paul was my place of birth in March 1893. My graduation at 18 proved an epochal time in my life, for I was converted to a Christian faith in the living Christ who became my guide in the important years ahead.

I became a Junior Intern at Bethesda Hospital in St. Paul where I obtained acquaintance with men of ability and integrity who upheld the reputation of their profession, and after my graduation from the University of Minnesota in 1917 I received an appointment to serve as First Resident in Tuberculosis with Dr. Longstreet Taylor.

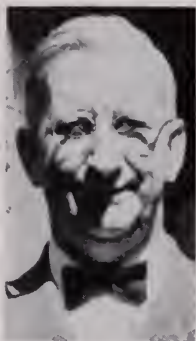
My name was entered on the roll of World War I veterans as a first lieutenant, though I was shortly discharged after the signing of the Armistice. I then accepted the position as City Physician for St. Paul, entered private practice, continuing in that capacity up to the present date.

It is my hope and prayer that, as God permits, I may show forth his praises and be ready always with meekness and fear to give an answer to all who may ask the reason of the hope within me. I am convinced after 50 years of medical practice that along with advice, drugs, surgery, diet and all forms of treatment, the greatest therapeutic measure at our disposal is prayer and I believe that it is of real importance that we recognize Christ as the Great Physician, one whose hands hold all power in Heaven and on earth.

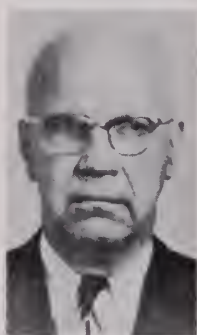


Herbert A. Molander, M.D.

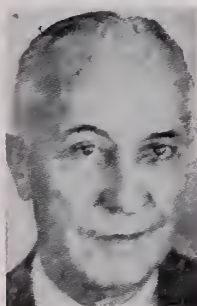
FIFTY YEARS



Gustaf T. Nordin, M.D.



Fritz R. Pearson, M.D.



Edwin F. Robb, M.D.



Andrew Sinamark, M.D.

When I graduated from the University of Minnesota Medical School in 1917 I made a resolution never to treat a patient unless I was satisfied that I knew what ailed him; if I didn't know, I was content to refer him to someone who did.

I was born in Almhult Smaeland, Sweden, in 1888, and emigrated to Minneapolis in 1905. I served my internship at the Swedish and Minneapolis General Hospital and thereafter received a commission as a First Lieutenant in the Medical Corps during the first World War.

I was married to Gertrude Jacobson in 1916, and during my absence in the War she served as a dietitian in the Deaconess Hospital until my return from France.

In 1919 I began practice in Minneapolis, but later studied radiology with Edward S. Blaine of Cook County and with Professor Forsell at the University of Stockholm during the fall of 1927, and also with Holzknecht in Vienna in 1928.

In January 1930 I discontinued my general practice to devote full time to radiology, and at the Swedish Hospital in Minneapolis I obtained the first 200,000 volt deep-therapy unit where I was the Director of the Department of Radiology.

After my retirement in 1956, my wife and I lived in California where I obtained a license to practice but never did so.

Dr. Pearson was born in Wisconsin, January 29, 1892, and graduated from the University of Minnesota in 1917. He has been very active in the Tuberculosis Clinic in the St. Paul Bureau of Health and has been responsible for the remission of this disease in this area.

I grew up in a small town in Missouri and lived next door to a young country physician who played catch with me, taught me how to throw curves and bat a ball. At that time I was 12 years old. I was making frequent trips into the country to "help" the doctor drive the team and set a broken arm. From this youthful experience the decision was made to become either a doctor or a big league ballplayer. The former won out.

After practicing pediatrics for 40 years in Minneapolis, I have now retired to Boca Raton, Florida, where life is most enjoyable but there are no kids next door with whom to play catch.

I am so grateful to the country doctor who influenced my life.

As a youngster I was proficient at fixing machinery on the farm; so I decided that I was cut out for an engineer. But in my second year at the University of Nebraska I flunked two subjects and then switched to a course in science, from which I graduated and then taught in a small college. However, I soon became convinced that I would never be a dedicated teacher.

I graduated from medicine at the beginning of the First World War and was immediately assigned to the Navy to do eye, ear, nose and throat work.

Later I endeavored to do general practice in my own home town but soon discovered that my friends and relatives remained with their own physicians.

Later the Veterans Bureau at Omaha offered me a position on the strength of my Navy experience, and within an hour I was on the job. During a leave of absence I studied in Vienna and found this to be one of the highlights of my life.

One day out of curiosity I stopped in at the Chiropractic College and was heartily welcomed as a prospect; but after spending a day visiting the classes and clinic, I knew sufficiently well that this type of healing was not for a medical man.

As I retire I look forward to reading books, an avocation I have deferred for many years.

FIFTY YEARS

I graduated from the University of Minnesota Medical School in 1917, served one year as an interne at the Anchor Hospital and was then in the United States Navy Medical Corps for another year. Subsequent to that I located in Stillwater in 1920, where I remember my first obstetrical patient as a transverse position.

I had no help except grandma holding the old-fashioned kerosene lamp. The husband was unable to tolerate the ordeal and took the lantern into the barn to do the chores while I proceeded with the delivery, chloroform container in one hand and a sterile glove in the other. Everything seemed to be progressing nicely until the lamp chimney tipped to the floor. Grandma then ran to the barn to obtain the lantern as we finally succeeded in delivering a healthy baby.

Early the next morning the mother was up preparing breakfast. "Early ambulation" in its infancy.

I have always asked God to help in difficult cases and I feel that the daily devotions that I have shared with my wife and church have helped me immeasurably in my work as a doctor.



John W. Stuhr, M.D.

Since you allow a considerable amount of leeway in the anecdotal-type of biography, I must say that the epochal incident in my life was the meeting and marriage of my staid New England Puritan Grandfather Sweetser to my Grandmother Kelley from Elphim, Ireland. Imbued with such genes, my father came west in the 80's and married another Irish girl named Higgins from Prince Edward Island, and in due time, just after World War I, I too married an Irish girl from Minnesota. We have lived happily together ever since. She can testify to the persistence of those New England characteristics which can be seen in both our children and our grandchildren. My son, Ted Jr., practices with me in Minneapolis.

If I were to follow the admonition of writing with the help of my wife, she might put some Irish glamour into the description of a professional anecdote.



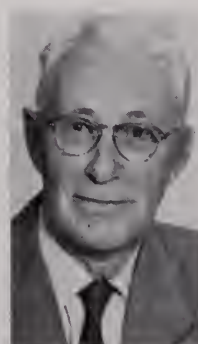
Theodore H. Sweetser, M.D.

I graduated from the Manitoba Medical School in 1917, and during the last year of schooling we were registered as privates in the Canadian Army without pay; but upon graduation we received our majority. I was then promptly discharged because of iritis and subsequently served as locum tenens during the influenza epidemic of 1919.

From 1923 to 1925 I served a Fellowship at the University of Minnesota and thereafter practiced at the Newark Clinic until it was dissolved.

In 1947 I became the Medical Director of the Minnesota Mutual Life Insurance Company and finally retired in 1958 to Ely, Minnesota, where during the summer months I spend some time in the office of Dr. O. E. Sawyer while he takes a short vacation.

I expect to retire completely in May, 1967.



Alexander E. Venables, M.D.

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Curbstone Consultation

Ventricular Hypertension

QUESTION: I have heard that right ventricular hypertension may produce chest pain similar to angina pectoris from coronary atherosclerosis. By what mechanism is such pain produced?

ANSWER: The systolic pressure in the right ventricle is normally lower than the aortic diastolic pressure. For this reason right ventricular coronary flow continues throughout systole, whereas the left ventricular coronary flow ceases. When the right ventricular systolic pressure is elevated, ischemia can be anticipated associated with a reduced coronary flow.

Angina pectoris does not usually occur in cases of ventricular septal defects associated with pulmonary stenosis in which the right ventricular pressures are also elevated. Therefore, right ventricular hypertension cannot be the only factor involved. When the interventricular septum is intact the diastolic pressure in the hypertensive right ventricle may exceed the diastolic pressure in the left ventricle. With the existence of a large interventricular septal defect the pressures in the left and right ventricles remain equal throughout the cardiac cycle. These diastolic pressure relationships on cardiac collateral circulation may account for angina pectoris occurring only in patients with right ventricular hypertension that have an intact septum.

The best explanation for angina pectoris occurring in patients with right ventricular hypertension, therefore, seems to be on the basis of ischemia of the right ventricle secondary to reduced coronary flow resulting from elevated right ventricular pressure during both systole and diastole.

Harold D. Kletschka, M. D.
Syracuse, New York

Too Long!

It took the world from the day of its creation to the time of the sixteenth century to raise a doubting Thomas of sufficient mental strength and courage to state that questions were answered not by authority, but by experiment. — Charles Mayo

Five per cent of the people think, ten per cent think they think, and all the rest want a slogan so they don't have to think.— Spuck Tidings

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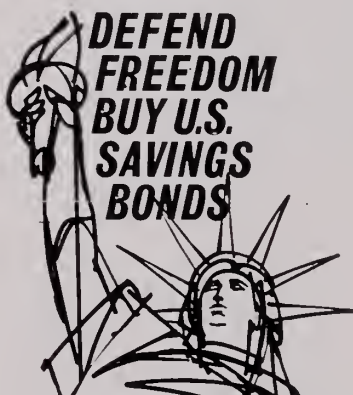
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Therapeutic Effects: Stiffness and pain may diminish within 2 days, and full mobility may be restored within a week. These effects are obtained with oxyphenbutazone alone or combined with physiotherapy or local hormonal injections. The drug is usually well tolerated and does not affect pituitary-adrenal function or immune response.

Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently.

Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage. Make regular blood counts. Discontinue the drug and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The most common are nausea, edema and drug rash. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, or a generalized allergic reaction may occur and require withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

Dosage in Painful Shoulder: 600 mg. daily in divided doses for 2 to 3 days; 300 mg. daily thereafter. Usual duration of therapy: 2 to 7 days.

Availability: Tablets of 100 mg.

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The Viewing Box

Man with Stiff Joint

A MAN, 56 years of age, was injured six months prior to his x-ray when his right leg was trapped between two hot metal billets, his clothes caught fire and he sustained third degree burns over both legs. Burns were most prominent about the right ankle, where exuberant granulations subsequently developed. Following debridement, two stages of skin grafting were successfully performed. This patient failed to regain normal ankle motion and ambulated with the aid of crutches.

At the time of these x-rays, examination revealed the grafted areas to be well healed with limited pliability suggesting moderate underlying fibrosis. Motion cannot be detected within the ankle joint, nor can inversion be performed. Dorsal flexion is limited to the talocalcaneal articulation, and motion is mildly restricted in remaining joints of the foot. There is no open drainage, and excellent pulsation is present in the dorsalis pedis artery with sensory testing normal peripherally.

What is your diagnosis? (See next page.)



A. P.



Lateral



Oblique

DIAGNOSIS: Bone and Joint Changes Following Burns

Serial x-rays in the severely burned patient may reveal changes in the bone and joint which can act as a deterrent to remobilization. These changes may be subtle or may show progression from normal bone to advanced skeletal involvement. All major joints may be involved, particularly, the elbow, knee and ankle. As defined by Evans and Blumel, skeletal alterations which cannot be ascribed exclusively to the initial thermal insult, fall logically into four groups.

Alterations Limited to Bone

Osteoporosis is common to all severely burned patients and may appear as localized or generalized bone atrophy. Localized change may be very limited but of great intensity and appear with an abrupt onset. In these instances it is felt that a vasomotor reflex phenomenon contributes to a local hyperemic state. Atrophy of the generalized type may be secondary to hyperemia, chronic inflammatory process and prolonged inactivity. However, malnutrition with protein insufficiency and/or electrolyte imbalance and adrenal cortical hyperactivity may also be etiological factors.

Periosteal new bone formation may underlie areas of severe burn or may appear in conjunction with a destructive process in an adjacent joint, due to acute hyperemia or a chronic inflammatory process. It is known to persist until there is good skin covering and does not continue to proliferate after the skin has been covered. Usually it is detected two to eight months after the burn.

Alterations Involving Pericapsular Structures

Pericapsular calcifications lie in the planes of ligaments or overlying tendons, have no attachment to bone, and may appear as spotty or continuous calcified plaques. They occur in both children and adults often as early as the second post-burn month. The precipitating causative factor is thought to be superimposed trauma with punctate hemorrhage in a localized area of tissue damage lying adjacent to the burn with mineral precipitation occurring in altered tissue pH. This type of spotty calcification may herald more serious joint impairment; however, it may not change and may disappear.

Osteophytes occur in adults and lie in the planes of ligaments at the site of bone attachment. Histological examination has shown that they represent simple new bone formation in fibrinous connective stroma, following superimposed minor trauma in the form of stress to a contracted and atrophic ligament.

Heterotopic para-articular ossification is found to lie deep in the plane of the surrounding muscle without evidence of actual replacement of muscle substance. This ossification has been observed at the hip, elbow and shoulder in both children and adults. It usually lies adjacent to, or under a burn and may be associated with immobility and progressive bone atrophy. Thus, as in the paraplegic patient, it may follow the degeneration of muscle, tendon or pericapsular soft tissue and hence is related to this chronic inflammatory state and the demineralization phenomena of continued release of bone salts. It is felt that the severely burned patient is constitutionally susceptible to minor trauma which may contribute to these pathological developments. Frequently this ossification occurs in the third month after the burn.

Alterations Involving the Joint Proper

Articular destruction and ankylosis are manifest early as capsular swelling, spotty pericapsular calcification and subchondral irregularity. As the destruction progresses, x-rays show soft tissue and intracapsular clouding, progressive destruction of the articulate surfaces, adjacent reactive periosteal new bone formation and ultimate bony ankylosis. Complete articular destruction may occur within a few weeks with resulting ankylosis within months. This is predominantly seen in children. The proximity of the joint to the burned area is not a constant factor in the genesis of intra-articular change. It has been postulated that this destruction may be due to bacterial invasion and this argument is supported by the knowledge that all severely burned patients have recurring transient bacteremia or septicemia of varying severity as long as there are open granulating areas. However, the clinical course is not typical of septic arthritis, and pathological examination has disclosed only panus formation and fibrinous adhesions without suppuration. Thus, it is more likely that the ankylosis is a degenerative process as it may occur in aseptic necrosis which may be initiated without bacterial invasion. It has been demonstrated that these changes may be minimized by early skin grafting and initiating active and passive exercises as soon as the condition of the patient permits. Should this not be feasible, less deformity will occur if the burned segments are placed in a functional position.

Alterations Secondary to Direct Involvement

Tangential sequestration or local bone necrosis will occur when a segment of bone is exposed by the burn, but any joint which is exposed will undergo septic destruction. Septic arthritis, articular destruction, and delayed ankylosis is the usual sequence.

The films reveal irregular pericapsular calcification in the peri-articular structures adjacent to the fibula and also the medial and posterior cortex of the distal tibia, mild varying periosteal thickening in the distal tibia and fibula, peripheral osteoporosis, subchondral destruction with clouding and early ankylosis within the ankle joint. A radiologist, when given a compatible history, will find these x-rays characteristic of that pathological change which may occur secondary to a burn.

Donald E. Dietrich, M.D.*
Duluth, Minnesota

*Department of Radiology, The Duluth Clinic, Ltd.

References

1. Evans, E. B. and Blumel, J.: Bone and Joint Changes Following Burns Research in Burns. Publication No. 9. Amer Inst Biol Sci 1962.
2. Evans, E. B. and Smith, J. R.: Bone and Joint Changes Following Burns. J Bone Joint Surg 41-A, 5:785, 1959.
3. Koepke, G. H. and Feller, I.: Physical Measures for the Prevention and Treatment of Deformities following Burns. JAMA 199:11:791, 1967.
4. Kolar, J. and Vrabec, R.: Periarticular Soft-Tissue Changes as a Late Consequence of Burns. J Bone Joint Surg 41-A:103, 1959.
5. Stepanek, V. and Dolecek, R.: The Skeletal Changes in Burned Patients. Radiol Clin 29:82, 1960.

Elbow grease is a standard prescription for success, but some men seem to get further using the soft soap.—Springfield Republican

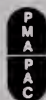
Power does not corrupt men; fools, however, if they get into a position of power, corrupt power.—Shaw

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facilities of medical schools and teaching hospitals. Such cooperation leads toward more effective care of more patients—the common goal of medical and pharmaceutical research—toward reduction in the cost of disease, toward increase in useful longevity.

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Tumor Conference

Thymic Cyst

TUMORS of the upper mediastinum, sometimes malignant and incurable, tend to defy identification of their origin. However, occasionally an upper retrosternal mass proves to be non-neoplastic and benign. The preoperative diagnosis, aided by appropriate radiographic techniques, can be made with some certainty and the organ of origin is readily identified under the microscope.

Case Report

A 26-year-old bricklayer saw his family physician, complaining of cough, sore throat and fever. Physical examination disclosed an upper respiratory infection in an otherwise robust young man. A chest film showed accentuation of the bronchovascular markings and a mass density in the right mediastinum. After his respiratory infection



Fig. 1 — P-A chest film showing a rounded mass density to the right of the ascending aorta.



Fig. 2 — On the lateral aortogram the anterior mediastinal mass, faintly outlined between arrows, does not fill with dye. (The streak across the sternum is an artifact).

Continued

had cleared the patient was referred to the thoracic surgery service, Minneapolis Veterans Administration Hospital, for further studies and treatment.

Physical examination and laboratory findings were normal. The medical history was negative except for two bouts of pneumonia during childhood. P-A and lateral chest films showed a rounded, 4 x 5 cm. anterior mediastinal mass, located to the right of the ascending aorta and intimately associated with it (Figure 1). On cinefluoroscopy the mass moved with the ascending aorta but did not pulsate expansively. An aortogram through the right femoral artery failed to show a communication between the aorta and the anterior mediastinal mass (Figure 2).

A right thoracotomy was performed. An encapsulated cystic mass, measuring 8 x 4 x 3 cm. was found between the superior vena cava, right atrium and ascending aorta. It was suspended on a 3.5 cm. long stalk which coursed into the area of the sternal notch. Cyst and stalk were completely excised. The patient recovered well and resumed work three months after the operation.

The histologic picture of the specimen was that of a thymic cyst. The stalk contained remnants of normal thymic tissue, composed of lymphatic and epithelial elements and Hassall's corpuscles (Figure 3). Much of the mass consisted of cysts filled with fluid and debris. The cyst walls contained many foreign body granulomas with giant cells and cholesterol clefts (Figure 4). Some cysts were lined with flattened and cuboidal cells in single and multiple rows. There was no evidence of malignant growth.

A mass in the anterior, superior mediastinum may originate in the thymus or in the thyroid gland, or it may be a teratoma ("the three T's"). Lymphoma, lipoma, fibroma, chondroma and angioma are less frequently found in this location. Rhabdomyosarcoma* of the anterior mediastinum is

*See Test Your Word Score Page 687.

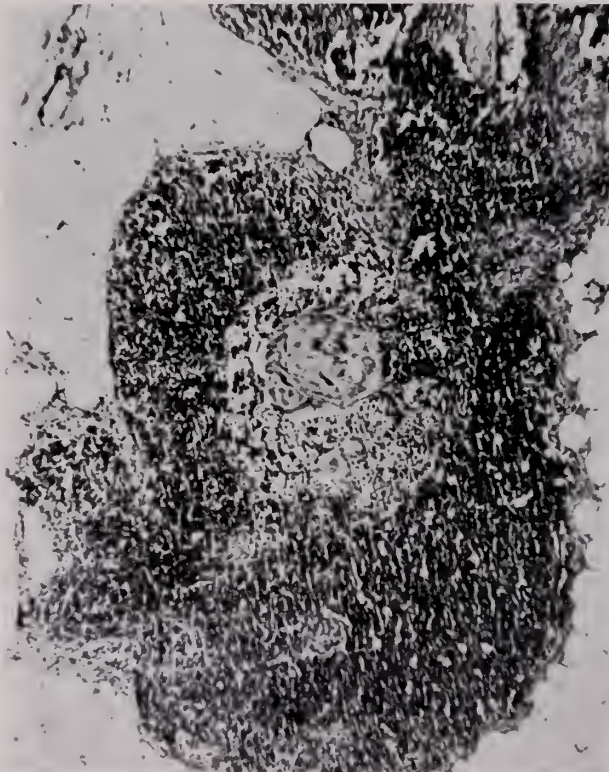


Fig. 3 — Section of the stalk, showing lymphatic and epithelial elements of normal thymic tissue. The epithelial cells are predominantly seen in the central portion, together with a giant Hassall's corpuscle and an accompanying smaller corpuscle (magnified $\times 40$).

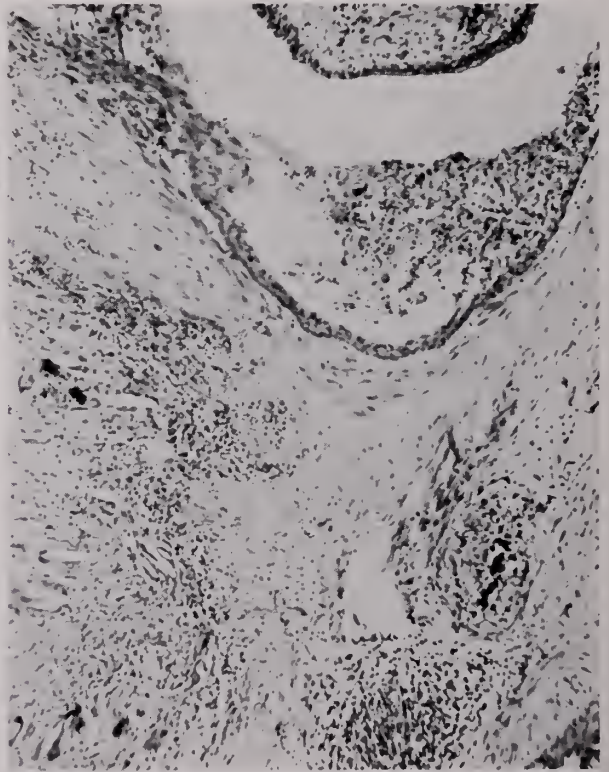


Fig. 4 — A section of the mass shows an epithelium lined cyst, a foreign body granuloma and cholesterol clefts in the left upper corner (magnified $\times 40$).

also rare. Some of these tumors show cystic degeneration or hemorrhage, especially when their rapid growth outstrips the blood supply. However, true cysts of pericardial or bronchial origin occur also in the anterior mediastinum. When the mass density lies in close contact with the aorta, as in the case of our patient, an aortic aneurysm must be excluded.

Some thymic cysts stem from embryonal rests which have migrated with the thymic anlage and are probably akin to dermoid cysts, originating in the thymus.¹ They are lined with flattened cuboidal or squamous epithelium. Other thymic cysts have no epithelial lining and are filled with debris, blood and cholesterol clefts. Castleman believes that they derive from degenerating Hassall's corpuscles.² A thymic cyst, in contrast to cystic thymoma, is by definition benign.

The microscopic picture of our specimen supports both theories of development. It shows: (1) cysts lined with flattened cuboidal cells, suggesting embryonal rests; (2) normal thymic tissue with a mixture of lymphatic and epithelial elements; and (3) Hassall's corpuscles of varying size, some of them degenerating with formation of cholesterol clefts and foreign body granulomas.

About one half of thymomas, solid or cystic, are associated with myasthenia gravis,³ and 15% of patients with myasthenia have a thymoma.⁴ This is not true for thymic cysts. A thymic cyst has lost almost all functioning thymic tissue. It is not neoplastic and represents incomplete removal of debris from the normal involution of the thymus.

H. W. Heupel, M.D., Ph.D.*
Minneapolis, Minnesota

*Department of Surgery, Veterans Administration Hospital and the University of Minnesota, Minneapolis, Minnesota.

References

1. Schlumberger, H. G.: Teratoma of the Anterior Mediastinum in the Group of Military Age. A Study of Sixteen Cases and a Review of the Theories of Genesis. Arch Path 41:398, 1946.
2. Castleman, B.: Tumors of the Thymus Gland. Atlas of Tumor Pathology, Section V — Fascicle 19, 76, 1955. Armed Forces Institute of Pathology, Washington, D. C.
3. Wilkins, E. W., Jr., Edmunds, L. H., Jr., Castleman, B.: Cases of Thymoma at the Massachusetts General Hospital. J Thorac Cardiovasc Surg 52:322, 1966.
4. Lyons, H. A.: Mediastinal Masses. Hosp Med 2:5, 1966.

Medical Men on Postage Stamps

Charles Laveran (1845-1922), French physician, pathologist, and parasitologist, Nobel Prize winner (1907), made valuable contributions to medical science in the fields of trypanosomiasis, leishmaniasis, and other protozoal diseases. His chief distinction lies in his continuation of the pioneer work of *Francois Maillot* (1807-1894) in the study of malaria and his eventual discovery of the parasite causing the disease. In 1954 Algeria issued postage stamps honoring both Laveran and Maillot.

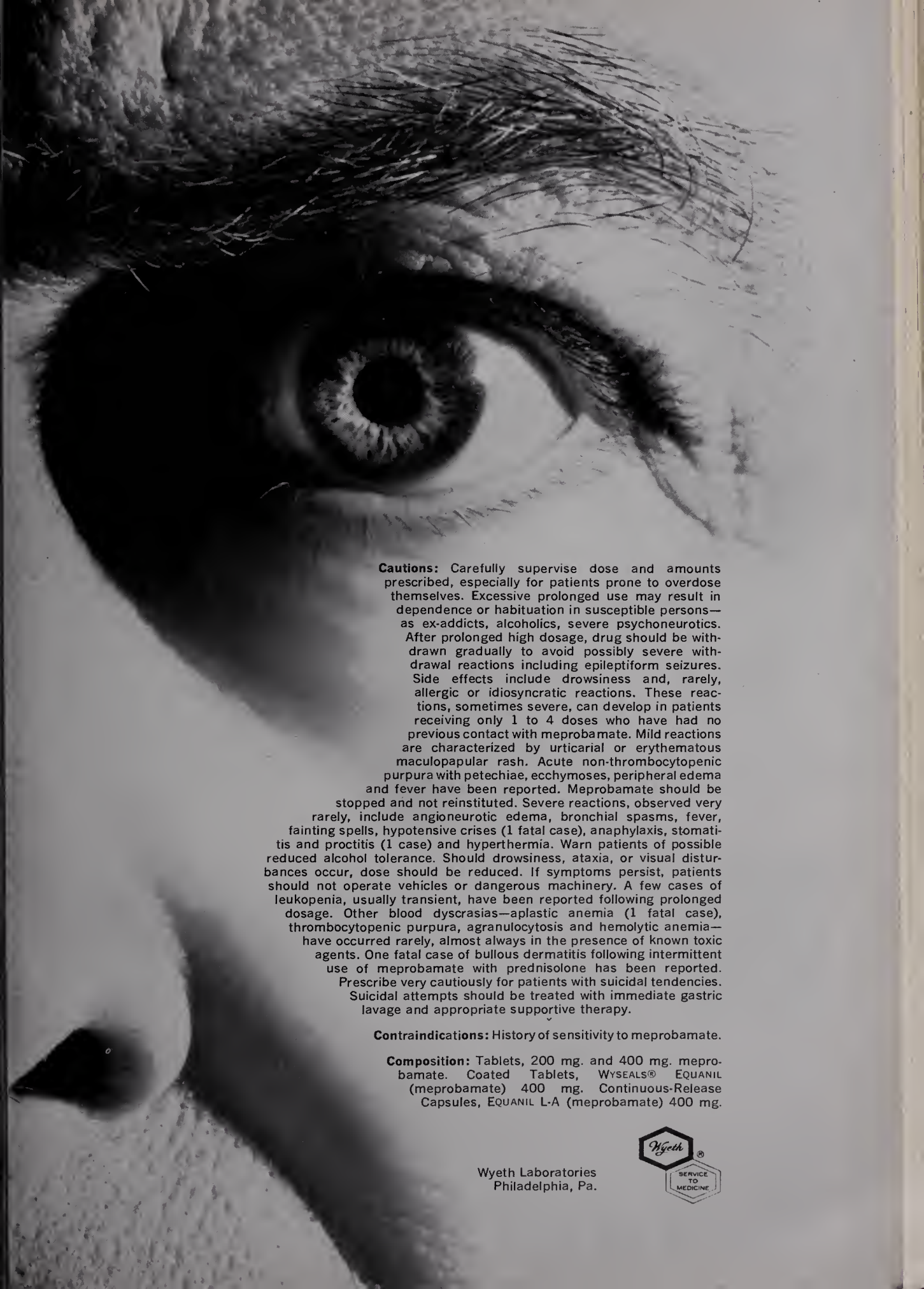
Alvaro Alvim (1863-1928), Brazilian X-ray specialist and martyr of science, was honored for his work and sacrifice by a postage stamp issued in Brazil in 1963.

How quickly in one morn is lost

What years have won with labour and with cost! — Petrarch

3 a.m.

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Cautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use may result in dependence or habituation in susceptible persons—as ex-addicts, alcoholics, severe psychoneurotics. After prolonged high dosage, drug should be withdrawn gradually to avoid possibly severe withdrawal reactions including epileptiform seizures. Side effects include drowsiness and, rarely, allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute non-thrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. Meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Warn patients of possible reduced alcohol tolerance. Should drowsiness, ataxia, or visual disturbances occur, dose should be reduced. If symptoms persist, patients should not operate vehicles or dangerous machinery. A few cases of leukopenia, usually transient, have been reported following prolonged dosage. Other blood dyscrasias—aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia—have occurred rarely, almost always in the presence of known toxic agents. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. Prescribe very cautiously for patients with suicidal tendencies. Suicidal attempts should be treated with immediate gastric lavage and appropriate supportive therapy.

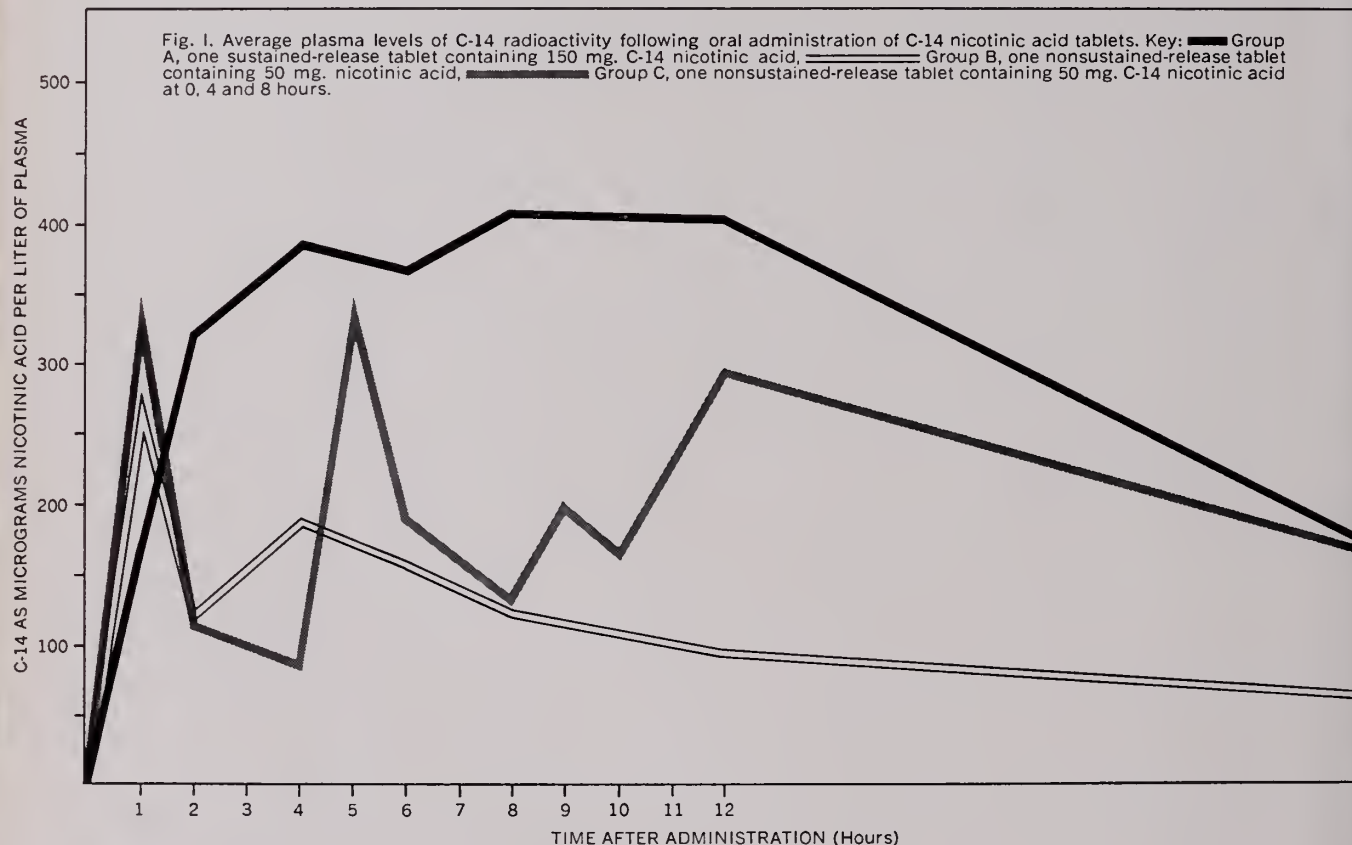
Contraindications: History of sensitivity to meprobamate.

Composition: Tablets, 200 mg. and 400 mg. meprobamate. Coated Tablets, WYSEALS® EQUANIL (meprobamate) 400 mg. Continuous-Release Capsules, EQUANIL L-A (meprobamate) 400 mg.

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absent-minded patients)

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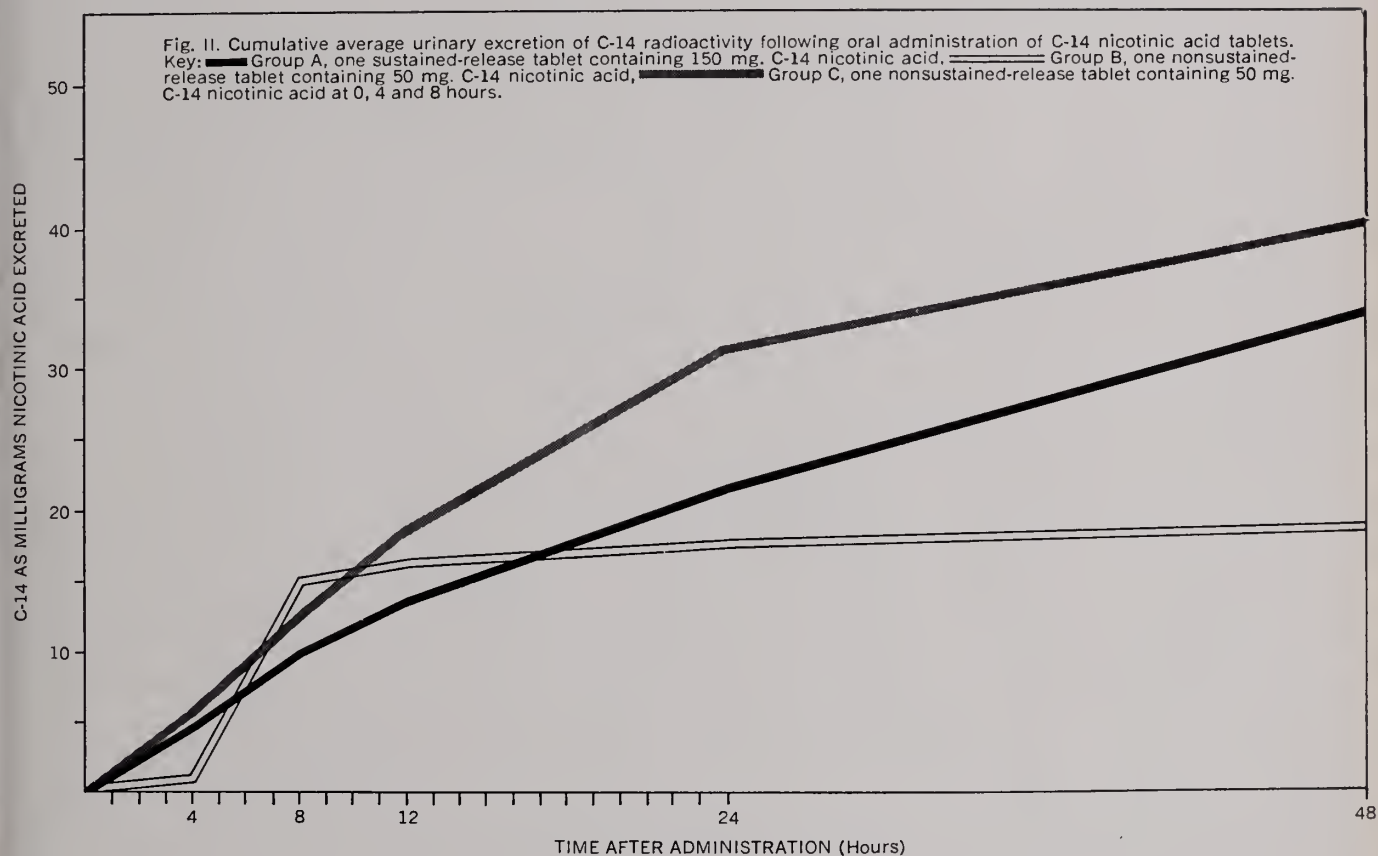
Such proven sustained activity makes the management of geriatric patients much easier by minimizing the possibility of neglected doses through absent-

mindedness or senile confusion. Therapy *can* be continuous on a daily dose of only one Geroniazol TT tablet every 12 hours.

The gradual release of nicotinic acid in Geroniazol TT will provide the well-known peripheral vasodilation needed in patients with deficient circulation and with a minimum amount (if any) of "flushing." Also, cerebrovascular circulation is complemented by pentylenetetrazol, long-established as a cerebral and respiratory stimulant.

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aged and debilitated



less confused and moody. Personal care, memory, emotional stability, social attention improve. Fatigue, apathy and irritability are reduced.

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Precautions: Exercise caution when treating patients with a low convulsive threshold.

Side Effects: Side effects are rarely encountered, however due to the vasodilatation effect of nicotinic acid, transitory mild nausea, flushing, tingling and pruritus are possible.

Dosage: One tablet every 12 hours.

Supplied: Prescribe bottles of 100 tablets, to take advantage of recent price reduction.

References: 1. Report by Nuclear Science & Engineering Corp., Pittsburgh, Pa., in files of Philips Roxane Laboratories. 2. Connolly, R.: W. Virginia Med. J. 56:263 (Aug.) 1960. 3. Curran, T. R., and Phelps, D. K.: Am. Pract. & Digest Treat. 11:617 (July) 1960.



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Neurological Conference

Huntington's Chorea*

Dr. Robert Soll:**

Patients with Huntington's chorea† often realize eventually that they have a disease which will render them mentally and physically incompetent. Not only do they have the problem of their own body deteriorating, but they also have family problems and fears that their children may inherit this condition.

History

Doctor Thomas Rolewicz:‡

The patient is a 44-year-old woman who has a family history of Huntington's chorea. Her symptoms of the disease began about five years ago when she noticed that she tired easily and was irritable. After extensive testing a tentative diagnosis of early Huntington's was made. Since that time there has been a general progression of her symptoms. She comes to us now not specifically for treatment of her disease but for help in alleviating the problems that the disease has brought upon herself and her family. The 17-year-old son is described by his father and mother to be different in recent years; for example, in the past two or three years he has been having so-called "psychic blackouts." For this reason, we were able to have him also referred by their family doctor. He is a very interesting part of the total problem since he is old enough to realize what is happening. They have a nine-year-old son, too; however, he appears to be less aware of the situation.

The family history revealed that the mother of the patient died in an institution, questionably by suicide. The patient's maternal aunt and two uncles also died of the disease. Another uncle, age 57, has signs of the disease now. Among the patient's siblings are a 42-year-old sister and two brothers, ages 35 and 33 years. The 42-year-old sister definitely has the disease and the 35-year-old brother also has suggestive symptoms as well.

Physical Findings

On physical examination one's first impression of the patient when she walks in the door is that she is inebriated, an aspect that has caused her much difficulty as far as her social relationships are concerned. Her general physical examination is well within normal limits. Neurologically there are small twitching movements of her fingers and restless movements of her legs. While sitting, she very skillfully attempts to portray

*Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatrics conferences are held every Wednesday from 1:00 to 3:00 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Charles Branthaver and Dr. Edward Defoe in Pediatrics, and Dr. Robert Soll, in Adult Neurology. Held March 10, 1966.

**Neurologist, University of Minnesota Hospitals.

*See Test Your Word Score Page 687.

‡Student Doctor, University of Minnesota Hospitals.

Continued

these movements as natural in order to prevent other people from noticing them; for example, she would hold onto the chair with her fingers to prevent their twitching or use seemingly normal movements to cover up the abnormal ones. She also has very coarse tongue movements which she cannot control. An intention tremor is present in her upper extremities, making it very difficult for her to light cigarettes or perform many household tasks. Also her gait is moderately ataxic. The deep tendon reflexes are brisk bilaterally but plantar stimulation produces plantar flexion in both feet.

The patient is currently taking reserpine 4.0 mg. four times daily and seems to tolerate it very well.

Dr. Soll:

An interesting point is that she deliberately wears low-heeled shoes because she has a great tendency to fall. Although her sister has had trouble coughing, our patient has not been bothered in this way; but chewing her food has been quite difficult for her. In addition to the abnormal movements of her tongue, some facial grimacing is also present.

Psychological Evaluation

Dr. John Brantner:*

We made no evaluation of the patient's intellectual status. We assumed that this is correlated with her illness and that its course is pretty well known. We focused more on the personality constellations in the family by giving the entire family the Minnesota Multiphasic Personality Inventory. The patient herself was able to take the test but she was extremely slow. After three hours she had finished only half the items. We used a technique of somewhat questionable validity: after she had finished one half the test, we assumed the results would be the same as though she had responded to the entire test; we then scored what she had done by doubling it to obtain the final score. It does, however, fit her quite well clinically. She was defensive but showed a pattern of bitterness and some fundamentally religious aspects of her personality. She appears to be completely free from overt depression. Instead, she is hysteroid, denying what the illness is really going to be like. Psychologically I consider this to be a form of deterioration, a very serious maladjustment. She is, I think, denying the depressive qualities of her disease by insisting that it is going to make no change; furthermore, she is struggling against it unrealistically. She continues smoking contrary to medical advice; she insists on driving her car and considers her insurance company unreasonable because they won't renew her policy. It's unfortunate that her involvement takes this particular form since her husband shows up on his Minnesota Multiphasic Personality Inventory as simply a mildly depressed, unhappy, somewhat anxious person — rather passive in his orientation.

The older boy's Minnesota Multiphasic Personality Inventory is relatively within normal limits for a 17-year-old. He is a somewhat animated, passive, and feminine type. He does not appear so when you see him; rather he looks like a large, rather masculine, athletic type; but I believe it has been reported that he has not done much dating. The only thing I can suggest from the multiphasic is an identification with his mother: a warmth and closeness to her which has been badly damaged by her gradual deterioration. The younger nine-year-old boy was given a picture test equivalent to the Minnesota Multiphasic Personality In-

*Associate Professor, Clinical Psychology, University of Minnesota Hospitals.

ventory: the Missouri Children's Picture Series. The results were within normal limits. Evidently he has not been influenced too much, as his personality does not show any gross deviations from an average nine-year-old.

Social Service Evaluation

Mrs. Diane Crespin:*

The patient lives with her husband and her two children; however, she is not able to care for the children or the house. Her husband is an assistant manager in a large business. They live in a suburban community and have a \$14,000 mortgage on their house, on which they are paying \$170 a month. They owe \$1000 to their local drug store for medications. Another major problem is the fact that both parents have recognized that their older son is quite disturbed. Apparently he has lighted fires around the house from time to time. In school he may get 100 one week and the next week, a failure. I spoke with the school to find out about his performance and they reported that he had an I.Q. of 135 on the Stanford Binet test. Essentially, his problem seems to be that of achievement. Although he tests well above average, in the tenth and eleventh grade he had only an average record. Concomitant with his mother's downhill course this year, his grade average has also fallen to almost that of a D student, that is, two F's, a D, an A and a B. For the most part he has failed to hand in assignments; yet he is well liked by the teachers and makes a very favorable impression. The school personnel had believed until recently that the patient had a drinking problem.

Another aspect of the family situation is the tendency for them to harken back to the "golden ages" when they had foster children in their home, when things were better financially. However, this doesn't seem to be the case, because the state allows only \$70 a month per child. Their caring for foster children began in 1959, about the time when the patient's physical problems first began. Interestingly, this project was initiated by the husband. In my experience, women usually have applied for children; therefore, one visualizes this case as the husband's way of coping with his wife's inability to manage around the house. Foster-children care by this family was discontinued in 1963, although the patient states that it was only this year that it was discontinued. The reason this family was taken off the list of foster parents was that their neighbors, who weren't familiar with the patient's problem, called in, complaining that she appeared to be under the influence of drugs or alcohol.

Neurological Evaluation

Dr. Soll:

The patient has followed the typical pattern of involvement observed in most patients who develop Huntington's chorea. The usual age of onset is in the latter third decade or early fourth decade, although rarely a patient can begin to manifest symptoms in the teens or as late as the sixties. Symptoms of irritability first appeared in this patient between age 39 and 40. An emotional alteration is encountered frequently as the initial change and eventual mental deterioration almost always occurs,

*Social Service Department, University of Minnesota Hospitals.

Continued

However, neurological signs such as muscle twitchings and choreiform movements may lag behind the psychic changes for months or years.

During her evaluation in neurology clinic, early dementia was readily apparent; for example, she was unable to subtract 7 from 100 and had an extremely short memory span. Also there was a notable tendency for her to ramble, as may be shown here today. Hyperactive reflexes have been reported to occur during the course of this disease. We would not consider this patient's reflexes to be anything more than brisk unless some associated evidence such as ankle clonus or a positive toe sign were also present. Her mild dysarthria is at least in part the result of abnormal movements of her tongue.

Pathologically, the areas of involvement in the brain that produce these changes are quite diffuse. In addition to the severe degeneration and secondary gliosis of the cerebral cortex, marked changes also occur in the basal ganglia, particularly the caudate nucleus and putamen. Genetically this disease is inherited as a Mendelian dominant; therefore, 50% of the offspring are likely to have the disease. Thus there is a real possibility that both of their children may not have the disease at all. On the other hand, either or both of them could have it.

Patient enters the room.

Discussion

Dr. Soll:

When did you first notice a change in your health?

Patient:

About three years ago. I was having trouble chewing and I couldn't eat. I was losing so much weight that I was down to 88 pounds. Every time our foster children came down with anything like a virus, I'd get it too. I finally figured it was Huntington's chorea. I was already decided to accept it.

Dr. Soll:

How did you decide to accept it?

Patient:

Well, I talked to our pastor and he said, "If in case you have to trust the doctors, that's what they go to school for." You see, at first I thought I needed a hysterectomy because my mother had a hysterectomy. She didn't need it because she had ulcers and she didn't need it. Of course, she was a little nervous.

Dr. Soll:

Is there anybody else in your family that is nervous?

Patient:

Yes, my sister has Huntington's chorea.

Dr. Soll:

When did you know she had it?

Patient:

She has had it a year.

HUNTINGTON'S CHOREA

Dr. Soll:

How is she now?

Patient:

Not very good. She has had all kinds of side effects. She is on the same pill I am taking.

Dr. Soll:

Does the reserpine seem to help you a lot?

Patient:

Yes sir, and even better is this pill that my doctor gave me this past Christmas. Anyway it has some appetite control. Everytime someone said something to me. I have two boys, and the one boy is a teenager. But anyway, everytime anybody said anything I'd be sitting at the table and they'd say, "Mother, what on earth is wrong with you?" and I'd sit there and try to tell them and I couldn't tell them — but every little thing that they said — you know, so that's why when I started losing so much weight, I took this before meals, and everytime I call up the doctor.

Dr. Soll:

From where was your family originally?

Patient:

England.

Dr. Soll:

Does anybody feel that you have been drinking?

Patient:

Yes, quite a few times. Last October when I was getting off the bus, the bus driver looked at me and said, "Are you sure that you aren't drunk?" and I said, "No, I am not drunk." I said, "I have Huntington's chorea," and he said, "Yeah, I bet you do." So anyway —

Patient Leaves the Room.

The Patient's Husband Enters the Room.

Dr. Soll:

When did you first find out that your wife had her illness?

Patient's husband:

I first recall in November, 1961, she was in the hospital and some changes came over her. She showed some symptoms or some reactions that weren't quite normal. This went on through the winter, but we still weren't exactly sure of what it was. In March, 1962, it was confirmed that she had Huntington's chorea. That's when it was first noticed that her tongue quivered and she still couldn't walk around normal.

Continued

Dr. Soll:

Was she aware of her mother's illness and that she might have similar troubles?

Patient's husband:

Yes . . . When her mother died in March, 1952, we were all put on the alert by my father-in-law. He told us that it affects the genes and that any one of the children could have it; consequently, he suggested that they all have frequent check ups.

Dr. Soll:

How has your wife's illness influenced your outlook on life?

Patient's husband:

Well, she has had a morbid outlook in general, but this is not exactly true — I mean at times it was kind of exasperating. Yet, I know that things could always be worse.

Dr. Soll:

How do you envision the future?

Patient's husband:

Well, for myself, I am on the downhill side in age now so it won't affect me a great deal. The children are my greatest concern now. I went through a similar case with my own mother; she died of cancer the same year that I graduated from high school. You kind of look at the parallel situation. I suppose it is something you should not do, but one does anyway.

Dr. Soll:

What would be the most help to you in easing these problems that you have?

Patient's husband:

She actually has such an erratic schedule — she stays up at nights, sleeps by the day, etc. I started to say that actually when she is awake, the thing that bothers me is that I don't like to leave her alone. One thing is her smoking and I am afraid of fires.

Dr. Soll:

Have you thought of commitment?

Patient's husband:

Well, I know it is coming and her symptoms have increased rapidly in the past six months. It can't be any other way.

Dr. Soll:

Do your children realize the significance of her illness?

Patient's husband:

Our older boy is pretty well aware of it, but our younger boy only

knows that his mother is ill and that she will get worse rather than better. Actually some of her reactions are like a child. I think our younger son senses this also when he has to treat his mother as an equal which she should not be.

Dr. Soll:

Do you think it has influenced the oldest boy's work in school?

Patient's husband:

I think it has some. He is one that doesn't talk a great deal.

Dr. Soll:

Has he had any counseling in his school work?

Patient's husband:

No. I don't think the school knew about his mother being ill until recently.

Dr. Richard Magraw:*

You indicated that you were sort of writing yourself off in this as being on the downgrade of life, and I got the impression that what you are attempting to do is arrange things the best way for the boys.

Patient's husband:

Well, yes, I figured that they have a future ahead of them and I want to make sure that they can get the better things out of life right from the start that they should have.

Patient's Husband Leaves the Room.

Dr. Soll:

Dr. Lowry, what problems have you had with the patient?

Dr. Janet Lowry:**

She has been treated by us since 1960. Her chief complaints have been bronchitis, nausea and vomiting. As far as her neurological status is concerned, I don't think it has changed much. Occasionally she has expressed what appeared to be paranoid ideas; for example, one time she felt that someone was poisoning her food. The situation must be very difficult at home because she obviously is so borderline that the family has trouble. They treat her as though she were still normal and they have trouble recognizing that she is different. I think it is understandable that her husband might become frustrated. I don't believe that she is able to do very much around the house. The family does all the grocery shopping, cooking, and cleaning.

Dr. Magraw:

What was the immediate reason for referring her here at this time?

*Director, Comprehensive Clinic, University of Minnesota Hospitals.

**Referring physician.

Continued

Dr. Lowry:

The drugstore wouldn't give her drugs because the family did not pay their bill.

Dr. Soll:

Has the husband ever approached you with the problem of what may happen in the future?

Dr. Lowry:

No. We think she should be committed, but he hasn't accepted this.

Dr. Frank Meelhuysen:*

Is there any pathological information regarding the mother who died?

Dr. Rolewicz:

I am in the process of getting this. Her father had been extremely depressed after learning that this was a hereditary disease, and according to the patient, he has gone to great lengths to get a family history. He wants to help if possible, so he is going to be sending me this information also.

Dr. Robert Howard:**

Are there any techniques now available that can tell us whether the youngsters will develop Huntington's chorea or is it just a matter of waiting for it to develop?

Dr. Rolewicz:

The fact that the older son has so-called blackouts and is doing poorly in school might be an early manifestation of the disease and not just a reaction to the psychological impact of the situation according to the pediatric consultant. This has not been proven absolutely, but it does not seem to be a purely psychological reaction in some cases.

Dr. Brantner:

Pearson's¹ work with families with a history of Huntington's chorea showed that about half the male children developed psychic disturbances in late adolescence and approximately half of those who developed psychic disturbances were reacting to the revelation of the risks they faced. In the others, of course, it was the precursor of the disease itself.

Dr. Soll:

Patterson et al.² suggested in 1948 the possibility of using electroencephalography as a means of predicting the future development of Huntington's chorea in offspring of afflicted parents. Interestingly, 19 out of 25 subjects, most of whom were in their teens, had electroencephalographic abnormalities. Whether such a test actually would have predictive value still remains uncertain since I do not believe a follow-up report has been published on these specific cases.

*Assistant Professor, Department of Physical Medicine and Rehabilitation, University of Minnesota Hospital.

**Dean, College of Medical Sciences, University of Minnesota.

Dr. Howard:

Are there any unusual chromosomes that can be recognized by modern techniques?

Dr. Soll:

I am not aware of any study concerning gross chromosomal changes in Huntington's chorea.

Voice:

Is there a sex difference in the inherited pattern?

Dr. Soll:

No really significant difference. One recent report in 1961 by Oltman and Friedman³ gave a slight predominance to women, however.

Dr. Meelhuysen:

Is there any geographic dominance?

Dr. Soll:

Probably not. The original report of Huntington's disease was published in 1872.⁴ Huntington had followed his grandfather, who was also a doctor, on his rounds through a town in New England. They had seen several patients whose ancestors had originally come from England. At the present time the disease is not localized or limited to families in that area, since it has occurred sporadically throughout the world and in many races. In fact, in some it has occurred without any hereditary background. Usually a history of previous family involvement of the disease is found, however.

The Management

Dr. Soll:

It is pretty apparent that this is an extremely difficult situation. There is very little hope for improving the patient's physical condition. At the present time reserpine is one of the few drugs known to offer some relief for the abnormal movements in Huntington's chorea, but this has been strictly palliative rather than curative.

In this instance our attention can be better directed toward the husband and the children in an attempt to give them support and counsel.

Dr. Rolewicz:

I requested a consultation from Dr. Lee Schacht who is a counselor in genetics in Public Health and has worked with problems similar to those faced by this family. In general, he counseled the father as to what to expect. Much of this information is contained in a little booklet on Huntington's chorea. He suggested that the father wait a while before talking to the younger son, but felt that after we made this evaluation we could talk to the older son. He is looking forward to being able to talk to both boys when we deem it necessary.

Dr. Brantner:

There is one problem which I think is capable of solution. It is quite

Continued

evident that everyone is going to accept the patient's continued deterioration until someone can take over. At the present time, however, she is determined to postpone this as long as possible for herself, and she will postpone it indefinitely if she can. I am certain that the family can be manipulated in some way so as not to oppose these goals. The family is denying wanting to get rid of her but is somehow also weakening her determination to keep going. I think these feelings could be channeled so that the entire family could be working together to diminish guilt and conflict in the future.

Dr. Soll:

How do you suggest that this be done?

Dr. Brantner:

By frank openness with the three intact members of the family.

Dr. Magraw:

First, I'd try to meet the husband's needs. This man appears to be either largely denying his problems or living in hope of her commitment. I would try to find out what this really means in his life.

Dr. Lowry:

I think the boy is finally facing reality; for example, he would say to her, "I don't want to hear anymore about your Huntington's chorea." In a way, I think they approached me to encourage the patient to leave the family.

Dr. Magraw:

Isn't there some other option — maybe some kind of domiciliary living such as a nursing home? I don't know how realistic a plan this would be but another possibility would be assistance from a visiting nurse.

Robert Soll, M.D.
University of Minnesota Hospitals

Participating in the conference were: Dr. Robert Soll, Neurologist; Mrs. Diane Crespín, Social Service Department; Dr. Richard Magraw, Director, Comprehensive Clinic Program; Student Doctor Thomas Rolewicz; Dr. Frank Meelhuysen; Assistant Professor, Department of Physical Medicine and Rehabilitation; Dr. Janet Lowry, Referring Physician; Dr. Robert B. Howard, Dean, College of Medical Science; and Dr. John Brantner, Associate Professor, Clinical Psychology.

References

1. Pearson, J. S., Peterson, M. C., Lazarte, J. A., Blodgett, H. E., and Kley, I. B.: Symposium on Huntington's Chorea: An Educational Approach to the Social Problem of Huntington's Chorea. *Proc Mayo Clin* 30:340, 1955. 75:164, 1959.
2. Patterson, R. M., Bagchi, B. K. and Test, A.: The Prediction of Huntington's Chorea. *Amer J Psychiat* 104:786, 1948.
3. Oltman, J. E., and Friedman, S.: Comments on Huntington's Chorea. *Dis Nerv Syst Suppl* 22:313, 1961.
4. Huntington, George: On Chorea. *Med Surg Reporter* 26:317, 1872.

Nettle

The nettle is a good medicine for them that cannot breathe unless they hold their heads upright, and being eaten boiled with periwinkles it makes the body soluble. — Gerard

A large, dark, high-contrast microscopic image showing numerous spermatozoa. The sperm heads are bright and oval-shaped, with long, thin tails extending outwards. They are scattered across the frame, some appearing to be in motion. In the upper left corner, there is a smaller, square inset image showing a different view of the same or similar material, possibly a higher magnification or a different sample.

New view of an oral contraceptive at work

Although suppression of ovulation remains the primary mode of action of oral contraceptives, newer knowledge indicates that products like Norinyl-1 — which provide the combined action of both low-dosage progestogen and estrogen for the full treatment cycle — offer multiple contraceptive action that helps explain their unexcelled record of effectiveness. This report explores the secondary protective mechanisms against unwanted pregnancy offered by combined hormonal administration and the importance of the progestational agent in making such multiple contraceptive action possible.

Accumulating evidence has indicated that sparse, highly viscous cervical mucus has an adverse effect on the motility and survival of spermatozoa.

The estrogen-opposing progestational ingredient of Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.) reverses the usual mid-cycle picture of a thin, watery cervical mucus. The result — a built-in barrier that inhibits sperm from reaching the ovum should one be released. The inset in the adjoining photograph shows immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

How the estrogen-opposing action of Norinyl-1 creates a hostile cervical mucus

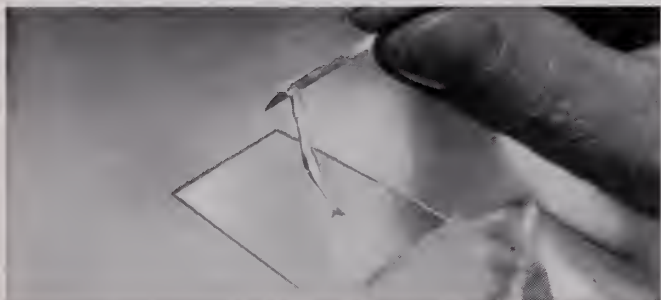
Normally estrogen activity during the fertile midcycle stimulates the production of cervical mucus. The mucus at this time is profuse and watery—allowing maximum sperm motility and promoting penetration.

But what happens when Norinyl-1 is administered? Its potent progestogen, norethindrone, opposes estrogen stimulation of cervical mucus. Consequently, the amount of mucus decreases and its viscosity increases. This results in a sparse but thick mucus barrier that diminishes the vitality of the sperm and impairs its powers of penetration.

How hostile cervical mucus supports contraceptive action

The importance of these observations to the effectiveness of Norinyl-1 has been noted in a report on 89 patients taking this medication.* In all instances, cervical mucus obtained from cycle day 5 to cycle day 29 appeared scant and thick and exhibited little or no Spinnbarkeit. In the opinion of this investigator, the effect on cervical mucus may be sufficient to prevent conception. *Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965.

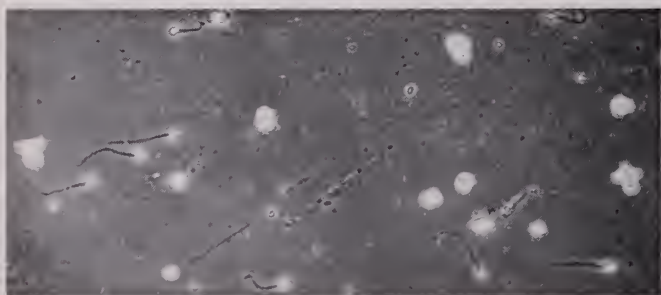
Normal cervical mucus at midcycle in untreated patient permits sperm motility... promotes sperm penetration.



Cervical mucus is thin and watery with a stretchability (Spinnbarkeit) of 15 to 20 cm.



Thin, watery mucus crystallizes into this well-defined, fernlike pattern within a minute.

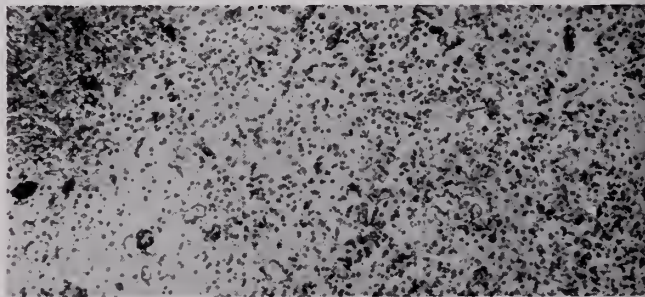


Spermatozoa appear healthy, are active and freemoving.

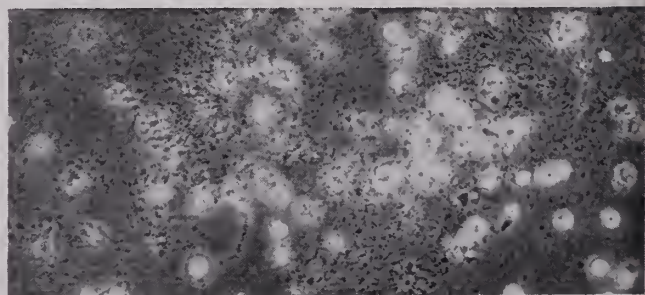
Hostile cervical mucus at midcycle produced by Norinyl-1 impairs sperm vitality... inhibits penetration.



Cervical mucus is scanty, thick and viscous. Spinnbarkeit is 1 cm. or less.



In thick, hostile cervical mucus the fern pattern is poorly defined or absent.

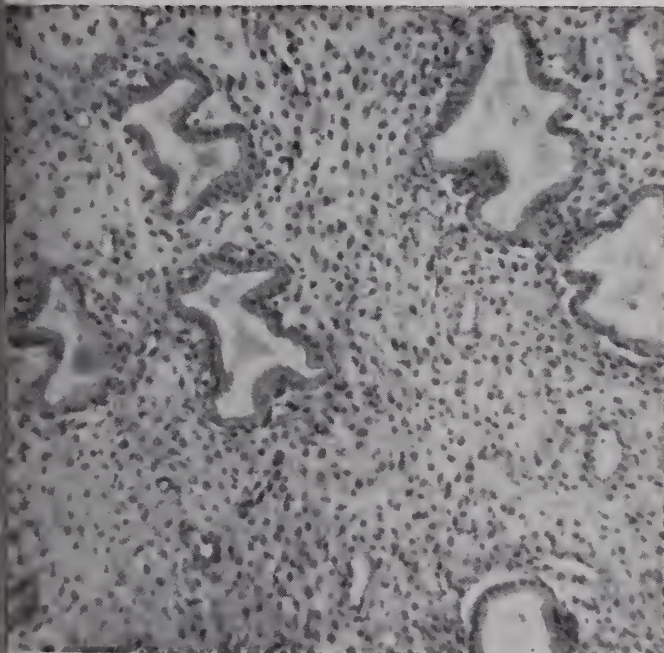


Immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

An endometrium unreceptive to nidation—another supporting contraceptive action of Norinyl-1

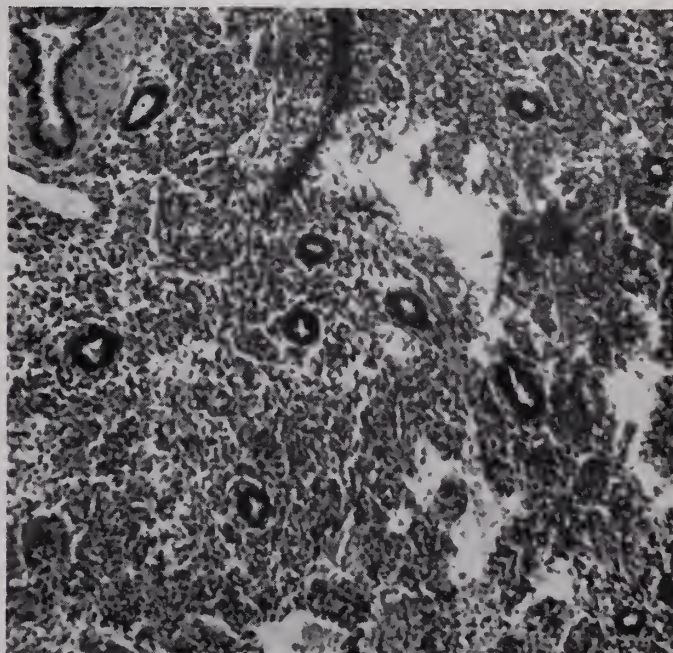
Let us suppose that an ovum is released—as occurs in an occasional, rare case—and somehow a sperm succeeds in penetrating the cervical mucus barrier? Should this come about, one additional action of Norinyl-1 may protect the patient from unwanted pregnancy—progesterone intake makes endometrial tissue unreceptive to implantation.

Endometrium of untreated patient



Normally the endometrium progresses through a proliferative phase stimulated by estrogen and a secretory phase stimulated by progesterone. During the secretory phase the endometrium is receptive to the fertilized ovum.

Unreceptive endometrium produced by Norinyl-1



When Norinyl-1 is administered its progesterone component—norethindrone—accelerates the secretory phase, suppressing glandular development. From day 11 on, secretory action is no longer present. The result is that during the latter half of the cycle the endometrium becomes unreceptive to egg implantation.

new
Norinyl-1
(norethindrone 1mg $\bar{c}$ mestranol 0.05mg) **tablets**

for multiple contraceptive action

effective fertility control
on half the previous dosage

maintains ratio
of the established
norethindrone/mestranol
combination

lower cost

new Norinyl-1[®] (norethindrone 1mg. $\bar{c}$ mestranol 0.05mg.) tablets

Reduction of oral contraceptive dosage to lowest effective levels has become a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now available in a new strength in which both norethindrone and mestranol are reduced 50 percent. Studies show that Norinyl-1 achieves fertility control with only 1.05 mg. of combined progestogen and estrogen per tablet.

Norethindrone was first reported for use as a progestational agent in human beings in 1955. Norethindrone 2 mg. with mestranol 0.1 mg., as an oral contraceptive, is currently in use by over 2,000,000 women. Clinical experience now establishes that Norinyl-1 also amply meets the criteria of reliability and safety.*

*Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965.

PRESCRIBING INFORMATION

Contraindications: 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

Warnings: 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of Norinyl-1 in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

Precautions: 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with Norinyl-1. Therefore, if such tests are abnormal in a patient taking Norinyl-1, it is recommended that they be repeated after the drug has been withdrawn for 2 months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibroids may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac, or renal dysfunction, require careful observation. 5. Although a cause and effect relationship has not been established, Norinyl-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, as in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are

indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged Norinyl-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Norinyl-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. A cause and effect relationship has not been demonstrated. 11. Because of the effects of estrogens on epiphyseal closure, Norinyl-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask the onset of the climacteric. 13. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

Side Effects: The following adverse reactions have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma, breast changes (tenderness, enlargement and secretion), loss of scalp hair, change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, erythema multiforme, erythema nodosum, hemorrhagic eruption, migraine, rash (allergic), itching, rise in blood pressure in susceptible individuals, mental depression.

The following occurrences have been observed in users of oral contraceptives. A cause and effect relationship has not been established: thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory results may be

altered by the use of oral contraceptives: increased bromsulphalein retention and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and but not extractable protein-bound iodine and decrease in T^3 values), metapyrone test, pregnanediol determination.

Other side effects reported to have occurred in association with use of this drug are dizziness, hirsutism, pains in legs, back, chest and abdomen, dysuria, drowsiness, vaginal discharge, libido increased and decreased, eruptions, hypermenorrhea, hypomenorrhea, increased appetite, G.U. infections, varicose veins, abdominal fullness, acne, headache, nervousness, allergies, blurred vision, pain in eyes, and itching in eyes. For complete clinical data, see package insert.

Dosage and Administration: 1. One tablet Norinyl-1 is administered orally for 20 days beginning on day 5 of the menstrual cycle (Count day 1 of the cycle as the first day of menstrual bleeding.) Repeat this dosage schedule for each cycle. 2. If no menstrual period occurs after a cycle of treatment (20 tablets) which patient adhered to the schedule, the patient must be instructed to resume taking the Norinyl-1 tablets 7 days after the previous day course was completed. For example, if the last pill of a previous cycle had been taken on Sunday, then a new cycle of treatment should begin on the following Sunday. 3. In the parturient woman, it is recommended that the first cycle of treatment should begin on day 1 of the first menstrual cycle. However, Norinyl-1 should not be administered during lactation.

Availability: Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.)—Dispensers of 20 and 60 and bottles of 250 tablets.

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INFLAMMATION: A cellular fight for life

A SYNTEX REPORT based on recently developed hypotheses about topical corticosteroids, including the cellular theories of inflammation by Thomas F. Dougherty, Ph.D., University of Utah.

You are looking at a fibroblast fighting for life. This cell—one of the most common found in connective tissue—has literally been poisoned by cytotoxins released from other cells that have ruptured. Soon, if the abnormal activity of this fibroblast does not cease, it, too, will rupture and die—one more casualty in the inflammatory wave of destruction precipitated by injury.

Until a short time ago no one had ever witnessed such a scene at the cellular level. Now, through advanced cinemicrographic techniques, it is possible to view and photograph the inflammatory process as produced experimentally in living animal tissue. This method permits new insight into the mechanism of inflammation and the role of corticosteroids in therapeutic management. Equally important, these techniques shed new light on factors that may make one corticosteroid more effective than another—factors that can be correlated with other chemical, biologic, and clinical parameters.

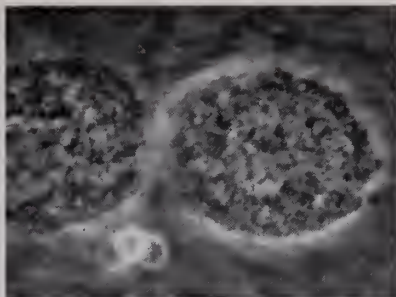


Visual evidence of how corticosteroids influence the inflammatory reaction

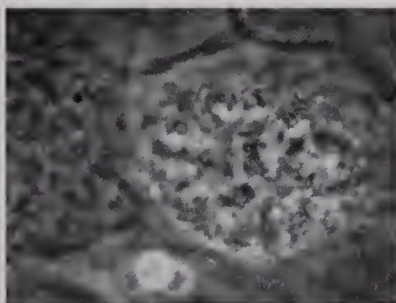
Working with phase-contrast cinematography on living animal tissue, Doctors Thomas F. Dougherty and David Berliner of the University of Utah College of Medicine have actually filmed cellular events that occur during the inflammatory reaction. This remarkable study* and additional work by these investigators, as well as by others, have established a new theoretical biologic basis for the antiinflammatory effect of the corticosteroids. (It must be noted that other theories, such as the lysosome or so-called "suicide bag" theory, have been postulated, although it is quite likely that there are more similarities than differences among the various theoretical models.)

The inflammatory wave of destruction

In this investigation an injurious injection of gelatin is used to set off an inflammatory reaction in living mouse tissue. What follows is a wave of destructive cellular activity that comprises the inflammatory response to injury. Mast cells (which contain heparin, serotonin and histamine) take up water, swell and rupture, releasing their contents, which are toxic outside the mast cell wall. These toxins, in turn, cause disintegration of other cells (such as fibroblasts) and the release of additional toxic material. Capillaries, too, take up water and leak unformed blood elements, causing edema. And polymorphonuclears, lymphocytes and perithelial cells invade the inflamed site. As a result of all these changes, the cellular environment reaches a state of turmoil.



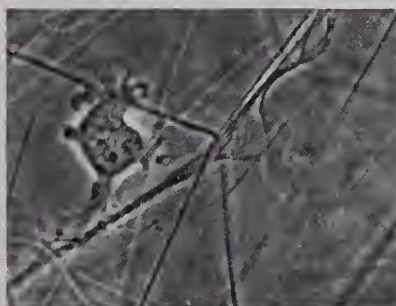
Phase-contrast microscopy showing mast cell before injury.



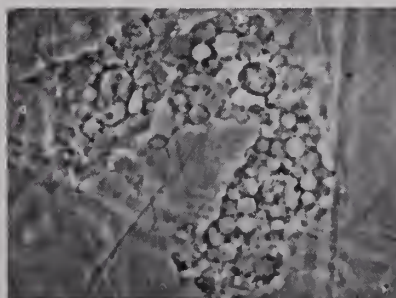
Mast cell (after injury) has broken up and released cytotoxins.

How corticosteroids change the picture

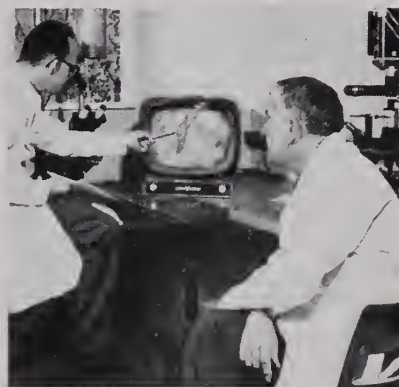
Corticosteroids appear to virtually stop the abnormal cellular activity that constitutes the inflammatory reaction. This permits the body's natural resources to clear up the inflamed area and repair the damaged tissue. This interpretation is supported by the fact that when the injurious gelatin solution is injected simultaneously with a corticosteroid — Synalar (fluocinolone acetonide) — the inflammatory pattern simply does not develop.



Fibroblast in high state of activity, much distorted.



Mast cells showing effects of corticosteroid action: cells are normal in size, shape and activity.

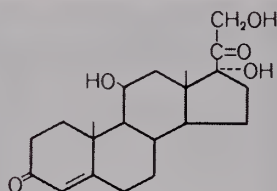


In summarizing his study Doctor Dougherty states: "...we also feel this work may explain why one corticosteroid helps a patient more rapidly and effectively than another. If it does, it is because one corticosteroid is the fastest, most effective inhibitor of the series of inflammatory events at the tissue level."

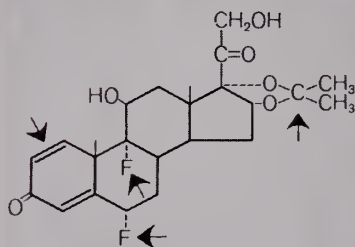
*A New View of Corticosteroid Action in Inflammatory Dermatoses, a film based on this study, is now available from your Syntex representative.

How advances in chemical design have achieved greater steroid potency

The chemical modification of corticosteroid molecules from the advent of hydrocortisone to the development of Synalar (fluocinolone acetonide) is a prime example of how biochemists can "design" to increase therapeutic activity and minimize undesirable side actions. Below, for example, we see the important changes that were made in reference to the hydrocortisone molecule to produce fluocinolone acetonide, one of the most active of all topical corticosteroids. As a result, a 0.01% preparation of Synalar (fluocinolone acetonide) has been reported to do the work of a 1% hydrocortisone product containing 100 times more corticosteroid. And it can often do it more effectively.



Hydrocortisone

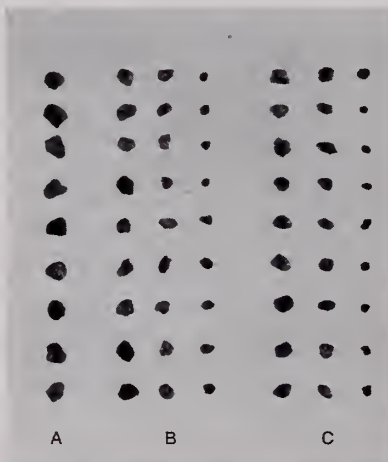


Fluocinolone Acetonide (Synalar)

- a double bond between carbons 1 and 2
- fluorine substitutions at both the 6- α and the 9- α positions
- the addition of the acetonide at the 16- α , 17- α positions, thus providing one of the most potent topical corticosteroids available.

How bioassay tests are used to "predict" therapeutic potential

Biologic assays are another tool used by researchers to help establish the relative activity of corticosteroids. To date no single method of assaying corticosteroid activity has emerged as the ideal "yardstick" for predicting therapeutic potential. Taken together, however, these methods have proved useful. When such tests are run on various corticosteroids, a definite order of corticosteroid activity becomes evident. Compounds with the highest order of activity may be expected to merit clinical trial to establish their high therapeutic potential. When assayed by these methods, fluocinolone acetonide (Synalar) emerges as one of the most active topical corticosteroids, milligram for milligram, available for clinical application today.



THE THYMUS INVOLUTION ASSAY¹⁻⁴ is run on adrenalectomized rats. The sizes of the glands are measured, and the degree of involution caused by the steroid is determined as an indication of its potency. In the above photo, the comparative involution of thymus glands achieved with hydrocortisone and Synalar (fluocinolone acetonide) is shown. Untreated controls (A) show normal size. Group B—injected with 1, 2 and 4 mg. of hydrocortisone—show progressively smaller thymuses as does Group C—but with only 1/500th the dose of hydrocortisone.



THE ANTIGRANULOMA ASSAY¹⁻⁴ also utilizes adrenalectomized rats. Granulomas are induced by subcutaneous implantation of cotton pellets on either side of the thorax. The degree of granuloma inhibition achieved by a steroid reflects its potency. The above photo shows the inhibition of granuloma formation achieved with hydrocortisone and Synalar (fluocinolone acetonide). Untreated controls (A) show large, red granulomas adhering to the pellets. Group B, receiving hydrocortisone and Group C, receiving fluocinolone acetonide, show little, if any, granuloma formation. Fluocinolone acetonide produced the same effect as hydrocortisone with only 1/500th the dose. This assay, as well as the thymus involution assay, measures systemic rather than topical corticosteroid activity. Nevertheless, results by these methods correlate well with other assays and with the milligram potencies of topical steroids in current clinical use.

Worldwide clinical experience confirms the predictable therapeutic potential of Synalar

It is particularly gratifying that the promise of the advanced chemical design and high order of bioassay activity of Synalar (fluocinolone acetone) has been confirmed by widespread therapeutic application. Indeed, the impressive clinical response rate of Synalar has been documented in no fewer than 232 papers from 22 countries.

PRESCRIBING INFORMATION

For initiation of therapy: Cream 0.025%, 5 and 15 Gm. tubes, 425 Gm. jars; *for emollient effect:* Ointment 0.025%, 15 Gm. tubes; *for maintenance therapy:* Cream 0.01%, 15 and 45 Gm. tubes, 120 Gm. jars; *for intertriginous or hairy sites:* Solution 0.01%, 20 cc. and 60 cc. plastic squeeze bottles; *for infected inflammatory dermatoses:* Neo-Synalar® Cream (0.025% fluocinolone acetone, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes.

CONTRAINDICATIONS: Tuberculous, fungal, and most viral lesions of the skin, (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. **PRECAUTIONS:** Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for pro-

Representative Clinical Results with Synalar*

Efficacy Documented in over 4,000 Patients

Condition	Number of Publications	Number of Patients	Significant Improvement†
Contact Dermatitis	27	750	713
Eczematous Dermatitis	21	472	409
Seborrheic Dermatitis	18	442	426
Atopic Dermatitis	24	460	426
Psoriasis	36	1,699	1,510
Neurodermatitis	18	351	324
Total	144	4,174	3,808

*Complete bibliography on request.

†Expressed by the authors as excellent, very good, good, complete remission of inflammation, etc.

longed periods of time. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. When severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. **SIDE EFFECTS:** Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. The neomycin in Neo-Synalar Cream rarely produces allergic reactions.

REFERENCES: 1. Lerner, L. J., Bianchi, A., Turkheimer, A. R., Singer, F. M., and Borman, A.: Anti-inflammatory steroids: potency, duration and modification of activities. *Ann NY Acad Sci* 116:1071 (Aug. 27) 1964. 2. Idem: Comparison of anti-granuloma, thymolytic and glucocorticoid activities of anti-inflammatory steroids. *Proc Soc Exp Biol Med* 116:385 (June) 1964. 3. Ringler, A.: Activities of adrenocorticosteroids in experimental animals and man, in Dorfman, R. I.: *Methods of hormone research*, New York, Academic Press, 1964. vol. III, pp. 234-280. 4. Gubersky, V. R.: To be published.

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Medical Seminar

Pregnancy Associated with Heart Disease

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THE CONSIDERATION of heart disease associated with pregnancy has increased in importance within the past two decades. This is the net result of several factors, which include a decreasing incidence of therapeutic abortions formerly considered to be justified, an increase in the number of children who survive rheumatic fever, subacute bacterial endocarditis, and congenital heart defects, and the better control of infections, anemia, and toxemia. Today, heart disease is one of the leading causes of maternal morbidity and mortality.

According to the New York Heart Association,¹ diseases of the heart "... are here considered to include not only the structural changes found in the heart, pericardium and adjacent arterial structures but also such disturbances of the functions of the heart as are manifested by arrhythmia, by its ability to perform its function as a pump and by its tendency to give rise to abnormal sensations." The Association has further devised a widely used system of complete cardiac diagnosis, utilizing the following terms: etiology, anatomy, physiology, and class (functional and therapeutic).

In several large series²⁻⁷ reported since World War II the incidence of heart disease associated with pregnancy has varied from 1 to 3.7% (Table 1). These reports indicate that more than 80% of cardiac problems associated with pregnancy are of rheumatic

origin; congenital and hypertensive heart diseases account for most of the remaining 20%.

More than 75% of rheumatic heart disease is mitral valve disease; another 10 to 15% is combined mitral and aortic disease.

A number of other types of heart disease are occasionally encountered in pregnancy and should be kept in mind. These include kyphoscoliotic* cardiac changes,⁸ subacute bacterial endocarditis, acute rheumatic fever, cor pulmonale, myocarditis (luectic, tuberculous, idiopathic), cardiovascular syphilis, chronic constrictive pericarditis, and Marfan's syndrome.⁹ In addition, a physician should always be prepared to handle a cardiac arrest.

Physiology

Perhaps the fundamental concept to keep in mind is that pregnancy is a complication of heart disease; the latter remains the primary problem and must be treated with full knowledge of those cardiovascular and respiratory changes that accompany pregnancy. The point to be made in the following discussion is twofold: first, the work of the heart in pregnancy is increased, and second, there are many normal physiologic changes that mimic the abnormal changes found in the pregnant cardiac patient.

Plasma and Red-Cell Volume

Both the major components of blood, the

Continued

*See Test Your Word Score Page 687.

red cells and the plasma, may be measured by the dye-dilution principle. Neither Evans blue nor radioactive iodinated serum albumin (nor any of the several other tracers used) cross the placental barrier; so measurements are of maternal plasma only. Red-cell volume may be measured by the same principle, by the labeling of a sample of the subject's blood with ^{51}Cr or ^{32}P .

From their extensive survey of the literature from 1938 through 1963, Hytten and Leitch¹⁰ arrived at the best estimates they could make for the increase in plasma and red-cell volume. These two components need only be added together to give the best estimate for total blood volume, which they conclude increases by 20 to 40%, with the maximum occurring from the thirtieth through the thirty-fourth week of pregnancy (Table 2). The validity of this statement has recently been questioned by Pritchard¹¹ (as well as others) who reported that he found no decrease in blood volume during the last weeks of pregnancy.

Body Water

Total body water increases throughout pregnancy, the amount being approximately 20% above normal at term. The mechanism of this increase has not been well established, but it appears to involve some, or all, of the following factors: sodium retention, increased plasma volume, depression of the glomerular filtration rate, decrease in concentration of serum proteins, and the action of estrogen and progesterone on the renal tubule.

Edema in the absence of preeclampsia or organic heart disease is common during the latter half of pregnancy and has been attributed to lymphatic and venous obstruction by the enlarging uterus, reduction in plasma osmotic pressure, and retention of water and sodium. As plasma volume increases, blood viscosity decreases and circulation time is prolonged.

The Blood Cells

The red cell itself apparently is changed

TABLE 1
Incidence of Heart Disease Associated With Pregnancy

Reference	Year	Percentage of Pregnancies	Type of Associated Heart Disease, %		
			Rheumatic	Congenital	Hypertensive
Fitzgerald and Associates ² (Cook County Hosp., Chicago)	1951	1.6	92.6	1.0	7.4
Ullery ³ (Pennsylvania Hosp.)	1954	1.12	81	4.6	11
Gilbert and Associates ⁴ (Lewis Memorial Maternity Hosp., Chicago)	1957	1.63	90.7	9.3*	9.3*
Burwell and Metcalfe ⁵ (Boston Lying-In Hosp.)	1958	2.3	85.0	12.0	1.0
Mendelson ⁶ (New York Lying-In Hosp.)	1960	3.7	91.0	4.3	2.8
Rovinsky and Guttmacher ⁷ (Mt. Sinai Hosp.)	1965	1.0	90	2.0	1.0

*Congenital and hypertensive diseases combined to make up 9.3%.

TABLE 2
Composite Estimate of Plasma and Red Blood Cell Volumes From 28 Studies of Pregnant and Nonpregnant Patients (1938-1963)¹⁰

Volume	Nonpregnant	Pregnant			
		20 wk.	30 wk.	34 wk.	40 wk.
Plasma, ml.	2,600	3,150	3,750	3,830	3,600
Red Blood Cell, ml.	1,400	1,450	1,550	1,600	1,650
Total Blood Volume, ml.	4,000	4,600	5,300	5,430	5,250

little by pregnancy and probably contains the same amount of hemoglobin as in the nonpregnant state. However, because the increase in plasma volume is relatively greater than the increase in red-cell volume, the hemoglobin concentration falls. The leukocyte count begins increasing at approximately the eighth week and gradually reaches its peak of 10,000 to 15,000 per cubic millimeter at term. In general, concentrations of electrolytes fall, the decrease being approximately 5 mEq. per liter for both cations and anions.¹² The total concentration of serum proteins decreases sharply, mostly in early pregnancy and due chiefly to a decrease in the albumin fraction.¹³ The significance of this change is unknown. The erythrocyte sedimentation rate begins increasing by the twenty-fourth week, the average corrected figure at term being 30 ml. per hour; the significance of this change is also unknown.

Pulse Rate and Blood Pressure

Several studies of the average resting pulse rate in pregnancy indicate that the rate begins to increase in the first trimester and peaks at approximately 88 beats per minute during the thirty-fourth to thirty-sixth week. Thus there are more than 14,000 extra beats per day in the pregnant state. Values for systolic blood pressure remain essentially unchanged until term, when a slight rise is normally noted; diastolic pressure usually decreases in the first and second trimesters and rises again to normal at term. Venous pressure measured in the arms, as well as in the right atrium, remains unchanged. However, femoral venous pressure is somewhat increased, probably due to vena-caval compression by the enlarging uterus. Right ventricular pressure, pulmonary artery pressure, and pulmonary capillary (wedge) pressure remain unchanged throughout pregnancy.

Cardiac Output

Determination of cardiac output in pregnancy by the Fick principle is subject to large error. Studies to date, although at some variance, indicate that the cardiac output begins increasing in the third month,

reaches a peak of 30 to 40% above normal somewhere between the twenty-fifth and the twenty-eighth week, then gradually declines to near normal at term.¹⁰ The stroke volume also is increased in pregnancy, since cardiac output increases to a greater extent than does pulse rate.

Oxygen consumption begins to increase in the second month, peaking 10 to 20% above normal at term. This increase is due primarily to fetal and uterine metabolism. Since cardiac output increases in early pregnancy to a greater extent than does oxygen consumption, the arteriovenous difference is smaller until near term, when it again approaches normal.

The heart itself is displaced upward, forward, and laterally as pregnancy progresses; the point of maximal impulse is therefore felt in the fourth intercostal space at or to the left of the midclavicular line. Both S_1 at the apex and pulmonic S_2 at the base are accentuated. A systolic murmur, frequent premature ventricular contractions, and split heart sounds are common. Several roentgenographic studies indicate that the mean heart volume increases 10 to 15% between the first and the third trimester; but the significance of this observation — if indeed it is valid — is not known. In pregnancy the electrocardiogram shows a left axis deviation until late in the third trimester, when it may shift back toward the right. Other cardiographic changes occasionally noted in the various leads include flat or inverted T waves, deep Q waves, depression of ST segment, and low QRS voltage.

Pulmonary Vascular Bed

Changes in the pulmonary vascular bed increase the lung markings on chest roentgenograms. As the uterus enlarges and encroaches on the diaphragm, fine basilar rales may be noted. Decreased height of the thoracic cavity is compensated for by an increase in its anteroposterior and transverse diameters. Pregnancy causes no significant alterations in the profile of the lung volume: vital capacity and maximal breathing capacity remain unchanged; during the third

Continued

trimester, the functional residual capacity decreases slightly, but the decrease is compensated for by an increase in the inspiratory capacity. The dyspnea of pregnancy noted in the first and second trimesters by so many women without heart disease is probably related to overbreathing, with subsequent drop in $p\text{CO}_2$.¹⁴

Standard exercise tolerance tests throughout pregnancy in normal women as well as in those with mild heart disease fail to prove that pregnancy imposes an added burden to physical activity.

Adams,¹⁵ and Adams and Alexander,¹⁶ and Hendricks¹⁷ in their studies on hemodynamics in labor agree that during a contraction the cardiac output rises 20 to 30% and that the pulse and the blood pressure increase — left ventricular work therefore is increased, and that from 250 to 500 ml. of blood is extruded from the uterus. They further have stated that there is no cumulative effect through the three stages of labor and that pain and anxiety in part, or perhaps wholly, account for the changes observed. At the conclusion of the third stage both cardiac output and left ventricular work were found to be significantly increased over those recorded during the first and second stages; this was considered to be due to increased venous return.

Diagnosis

A few diagnostic pitfalls may be encountered in the cardiac patient who is pregnant; these pitfalls are represented by the development of a new disorder such as acute rheumatic fever or subacute bacterial endocarditis, or as congestive heart failure superimposed on the existing heart disease.

In a previously unexamined patient, the task of diagnosing heart disease may be somewhat confusing. A complete history must be taken, the physician keeping in mind the normal physiologic changes of pregnancy. On physical examination a heart murmur is the most frequently encountered problem. Gorenberg and Chesley¹⁸ go so far as to say that a systolic murmur may be found in every pregnant woman if she is examined often enough. The criteria of Burwell and Metcalfe⁵ are adhered to by many

when an attempt to distinguish the functional murmur from organic heart disease is made:

1. The presence of a diastolic murmur must be regarded as clear evidence of organic disease.
2. Unequivocal cardiomegaly, as shown by roentgen examination, is an acceptable sign of organic disease but seldom exists as the only sign.
3. The presence of a systolic murmur of grade 3 intensity or greater (on the basis of 6) usually indicates organic disease.
4. The presence of a severe arrhythmia, such as atrial fibrillation, atrial flutter, or complete heart block, always indicates organic disease.
5. Other unequivocal signs include a pericardial friction rub, true angina pectoris, a diastolic gallop rhythm, or a pulsus alterans, persistent bacteremia, and notching of the lower rib margins on a chest roentgenogram.

Ancillary studies may include anteroposterior, oblique, and lateral roentgenograms of the heart after barium swallow (if indicated), electrocardiogram, pulmonary function studies, venous pressure and circulation time, exercise tolerance tests, and even cardiac catheterization in those women who urgently require clarification to ensure proper management.

Management

In the management of the pregnant cardiac patient, three possible solutions present themselves. The first is interruption of the pregnancy — that is, therapeutic abortion. The second is improvement of the heart condition through surgery, and the third is medical management of the cardiac problem throughout pregnancy, labor, and the puerperium.

Management as well as prognosis in most clinics is based on the patient's performance in previous pregnancies and on her functional capacity prior to her present pregnancy according to the criteria of the New York Heart Association¹:

Class I patients are those with cardiac disease but without resulting limitation of physical activity. For them, ordinary activity

does not cause undue fatigue, palpitation, dyspnea, or angina.

Class II patients have cardiac disease that results in slight limitation of physical activity. Such patients are comfortable at rest, but ordinary activity results in fatigue, palpitation, or angina.

Class III patients have cardiac disease that causes marked limitation of physical activity. They are comfortable at rest, but less than ordinary activity causes fatigue, palpitation, dyspnea, or angina.

Class IV patients have cardiac disease that makes it impossible for them to carry on any physical activity without discomfort. Symptoms of cardiac insufficiency are present even at rest. Any physical activity undertaken increases discomfort.

Therapeutic Abortion

There is some philosophic variance of opinion among those who have had experience with large numbers of pregnant cardiac patients.

Mendelson⁶ has stated the belief that the procedure is justified in the face of serious cardiac incapacity not amenable to surgery; however, he is willing to rely on supportive measures when religious or other special considerations are involved. Burwell and Metcalfe⁵ have recommended interruption of pregnancy only after careful study of the individual problem. They not only take into account the severity of the heart disease but also consider the special significance of a given pregnancy to a given patient. Rovinsky and Guttmacher⁷ strongly recommend therapeutic abortion for class IV patients, but believe that class II and III patients generally are better off completing the pregnancy. They too individualize their treatment somewhat.

In regard to rheumatic heart disease, Gorenberg and Chesley¹⁹ have stated that "if a patient . . . is seen early enough in pregnancy to be aborted therapeutically, she has been seen early enough to be given good prenatal care and thus be allowed to complete a successful pregnancy." Lund²⁰ has said that *therapeutic abortion is rarely, if ever, indicated* and should not be considered

until there is persistent or progressive disability after thorough, effective medical or surgical treatment or both. Gerbie and Skom²¹ are of the same opinion. They pointed out: "If the heart is in failure, interruption of pregnancy cannot be safely performed, and if the heart is compensated, interruption of the pregnancy is usually not indicated."

Improvement of the Heart Condition Through Surgery

Rapid and dramatic advances in cardiac surgery within the past 15 years have made it possible to improve the heart condition through surgery.

Mitral stenosis is the most frequent specific defect present, and experience in the handling of this lesion is, therefore, greatest. There is agreement on the advisability of *mitral commissurotomy for mitral stenosis*, when indicated in the nongravid woman in her childbearing years, because the burden of subsequent pregnancies usually is tolerated much better. But there is again some philosophic variance of opinion regarding the advisability of this procedure during pregnancy.

Surgeons and internists in general²²⁻²⁵ believe that commissurotomy is indicated in early gestation for heart failure or as an alternative to therapeutic abortion. Harken and Taylor²² prefer commissurotomy in patients who are borderline class III and IV, and they cite lower fetal and maternal mortality rates in operated patients, as contrasted to those managed medically. They also point out that therapeutic abortion done after commissurotomy, which is recommended by many, raises fetal mortality rate to 100%, subjects the patient to the risk of two operations, and is objectionable to many on religious grounds.

Mendelson⁶ has stated the belief that commissurotomy is indicated, if conception has already occurred, for patients with pure mitral stenosis and signs of pulmonary congestion. He favors cardiac surgery as soon after conception as possible so that the patient may benefit immediately, and so that there will be more time to resort to thera-

Continued

peutic abortion in the event of operative failure.

On the conservative side are Rovinsky and Guttmacher,⁷ Burwell and Metcalfe,⁵ and Gerbie and Skom.²¹ They consider commissurotomy for those patients who have severe intractable pulmonary congestion or edema early in pregnancy and who refuse interruption, or for those patients who after the fourth month are in heart failure or have pulmonary edema in spite of vigorous medical management. These authors point out that commissurotomy during pregnancy does not eliminate the hazard of rheumatic heart disease to mother and fetus in the present or in future pregnancies, that present-day medical management is effective for all but a few patients, and that the postcommissurotomy syndrome, atrial fibrillation, or embolic phenomena may develop.

Mitral insufficiency and the aortic valvular lesions are much less common and, even when found in pregnancy in their pure form, seldom cause trouble. Surgical repair imposes a far greater risk than does mitral commissurotomy, because it involves open-heart surgery with the use of cardiopulmonary bypass and usually involves insertion of a prosthesis. There is at least one case reported of Hufnagel valve replacement for severe aortic insufficiency that was followed by conception and a normal successful delivery by cesarean section.²⁶ The surgical mortality rate is 15 to 25%, however.

Often patients with severe congenital heart disease do not reach childbearing age; if they do, they rarely marry and have children. When successful corrective surgery has been undertaken prior to pregnancy, few problems are encountered. But the advisability of corrective surgery during gestation depends on personal opinion, the type of lesion, and primarily on its severity. Mendelson⁶ has stated that whenever indicated (that is, in severe uncontrollable failure, operable defect, reasonable risk) a repair during pregnancy should be undertaken prior to the peak cardiac load.

Ligation of a patent ductus arteriosus appears to carry the least risk but usually is not indicated unless uncontrollable heart

failure or subacute bacterial endocarditis develops. An atrial septal defect may be repaired during pregnancy but should probably be done only when heart failure cannot be medically controlled or when the patient declines therapeutic abortion. *Repair of a ventricular septal defect* is somewhat more risky, requiring open-heart technique. If the lesion is large and the danger of heart failure great, therapeutic abortion or medical management is recommended by Rovinsky and Guttmacher.⁷ They do not believe that there is any clear indication at the present time for correction of tetralogy of Fallot during pregnancy. Patients with pulmonic stenosis and aortic coarctation generally do well in pregnancy,²⁷ and unless progressive symptoms develop, surgery should probably be deferred until after delivery.

Medical Management

The medical management of the pregnant cardiac patient is based on two principles: the prevention of heart failure and its treatment, if failure should occur.

Prevention of heart failure revolves around reducing the avoidable work load on the heart. There are certain unavoidable loads placed on the heart of a pregnant woman that are maximal from approximately the twenty-eighth to the thirty-fourth week. This is, therefore, the critical period in the prevention of heart failure.

Restriction of physical activity is most important; Class I and II patients need not be greatly restricted but should have extra rest each day and should minimize house-keeping, stair climbing, emotional strain, and outside work. Class III patients require greater restriction, and Class IV patients must be kept at near complete rest in bed, either at home or in the hospital. For all classes, gain in weight should be kept to a minimum, especially in the obese, by low-calorie diets and low-sodium intake, the amounts determined more or less by consideration of class and clinical status.

Diuretics (thiazides) have assumed a major role in the management of the pregnant cardiac patient and are the mainstay of treatment for the pregnant woman with

hypertensive heart disease. Patients with moderate-to-advanced disease who show rapid or excessive gain in weight or evidence of venous congestion or fluid retention should receive orally administered diuretics. The use of parenterally administered diuretics, for example, meralluride, is indicated in acute or chronic heart failure during pregnancy.

Anemia adds to the circulatory load and should be treated promptly. Iron deficiency is the most common cause of the anemia; therefore large doses of iron, either orally or parenterally administered, are usually necessary. Careful transfusion of packed cells may be given to patients with severe anemia.

Since intercurrent infection is the most important precipitating cause of heart failure in the pregnant rheumatic patient, *antibiotic therapy is indicated at the first sign of infection*. Some clinics use prophylactic antibiotics throughout pregnancy in their rheumatic patients.

Hyperthyroidism can occur in pregnancy and is occasionally a factor leading to congestive failure. The possibility of hyperthyroidism should be kept in mind, for it is treatable by the use of antithyroid drugs or iodine or subtotal thyroidectomy. Radioactive iodine should not, of course, be used during pregnancy.

Congestive failure is most likely to occur when the cardiac load is maximal, that is, from the twenty-eighth through the thirty-fourth week. Lund²⁰ has stated: "Congestive failure is a medical and not a surgical disease and it should not be treated by cesarean section, hysterotomy, or induction of labor." Most authorities recommend immediate hospitalization and strict rest in bed if there is any indication of early heart failure, even a slight cough.

Digitalis is the most important drug in the treatment of heart failure and should be given whenever symptoms or signs of congestive failure appear during pregnancy. In the pregnant patient, digitalization should be carried out slowly over several days, but if necessary it may be done rapidly. This drug crosses the placental barrier, but

when used in therapeutic doses, it does not produce fetal distress. Maintenance therapy should be continued for class III patients but may be discontinued, with caution, in compensated class II women. Prophylactic digitalization of class II and III patients is practiced in some clinics for patients with a history of heart failure. Further treatment includes the measures previously enumerated for the prevention of congestive failure and may also call for the use of oxygen, morphine or meperidine, aminophylline, and rotating tourniquets or phlebotomy. One of the most serious complications of mitral stenosis in pregnancy is acute pulmonary edema. According to Mendelson,⁶ edema alone accounts for the greatest number of deaths of pregnant cardiac patients; it must therefore be treated promptly.

Labor and Delivery

It is now a well recognized principle that the pregnant cardiac *patient is best delivered vaginally*; if, however, an obstetric indication exists, *heart disease is only a relative contraindication to cesarean section*. The only exception concerns those patients with aortic coarctation. Some obstetricians believe that delivery in these cases is best accomplished by cesarean section. In the past, early induction of labor was commonly practiced; then cesarean section was considered the best means of delivery. Within the past 20 years, however, comparative studies have appeared that have indicated that vaginal delivery carries the least risk.^{5,6} Choice of anesthetic agent depends not only on the maternal and fetal status but also on the training and competency of the anesthesiologist. *Inhalation anesthesia probably is best* when conditions are ideal (good premedication, absence of respiratory disease, mature infant); but pudendal block or local infiltration may be the method of choice. Caudal and spinal blocks are effective but occasionally cause hypotension.

Hopefully, the cardiac patient beginning labor will be compensated; for this reason most clinics hospitalize their class II, III, and IV patients at least a few days before the estimated date of confinement, for reevaluation.

Continued

tion and treatment of their cardiac status. Antibiotics should be given prophylactically to rheumatic subjects, because there is often a transient bacteremia during labor.²³

As stated previously, the extra work imposed on the heart by labor has no cumulative effect, and the changes noted are considered to be primarily the result of excitement. In the first stage, therefore, good sedation should be maintained; the use of atropine and scopolamine is best avoided because each tends to produce, respectively, tachycardia and excitement. *A semireclining position for the patient is best.* The pulse and the blood pressure must be checked frequently; if the pulse rises above 110 beats per minute between contractions or if a cough, tachypnea, or dyspnea occurs, morphine and oxygen should be given and digitalization rapidly carried out. If the patient is not yet fully dilated when cardiac decompensation begins to occur, any means of effecting delivery will tend to aggravate the situation.

The second stage of labor should be shortened; or as Mendelson⁶ has said, "Prolonged straining to achieve the esoteric ecstasy of natural childbirth is not advocated. . . ." *Low forceps are advisable to shorten the second stage*, but extra care must be taken not to incur lacerations by application before dilatation is completed.

In the third stage *blood loss should be kept to a minimum* to avoid the secondary

strain of anemia. Large, intravenous infusions should be avoided; ergonovine should not be used because of its vasopressor effect; synthetic oxytocin is preferable due to its lack of vasopressor effect. Because immediate postpartum heart failure usually is caused by excessive blood loss, the treatment should include the Trendelenburg position and immediate and careful replacement of blood. Vasopressors should be used if blood loss does not seem to account for the heart failure. Occasionally, heart failure may occur between the fourth and the seventh postpartum day; the failure is associated with a delay in diuresis. Therefore, cardiac patients usually should be kept in the hospital at reduced activity for two weeks after delivery.

The so-called fourth trimester is the next dangerous period. A significant number of

TABLE 4
Deaths in Pregnancy Related to Classification*
of Heart Failure⁶

Class	Cases		Deaths	
	No.	%	No.	No. Due to Congestive Heart Failure
I	1,816	49	3	0
II	1,447	39	4	0
III	290	8	16	13
IV	147	4	8	7
Total	3,700	100	31	20

*New York Heart Association classification.

TABLE 3
Maternal Mortality in Pregnancy Associated With Heart Disease

Reference	Year	Percentage Mortality of Pregnant Cardiac Patients	No. of Deaths of Pregnant Cardiac Patients	Type of Associated Heart Disease		
				Congestive Heart Failure	Acute Congestion	Infection
Fitzgerald and Associates ² (Cook County Hosp., Chicago)	1951	3.4	24	21	2	1
Ullery ³ (Pennsylvania Hosp.)	1954	2.6	15	0	11	0
Gorenberg and Chesley ¹⁹ (Margaret Hague Maternity Hosp., Jersey City, N. J.)	1958	0.28	15	0	1	1
Mendelson ⁶ (New York Lying-In Hosp.)	1960	0.8	31	20	0	4
Ehrenfeld and Associates ²⁹ (Hadassah U., Israel)	1964	1.13	4	0	4	0
Rovinsky and Guttmacher ⁷ (Mt. Sinai Hosp.)	1965	0.5	1	0	1	0

women experience heart failure during this period; failure is probably due to the burden of resuming household duties. The term "postpartum heart failure" refers to an ill-defined syndrome that begins two to 10 weeks after delivery and is characterized by generalized cardiomegaly, signs of heart failure, and thromboembolism in the absence of any history of heart disease. It is apparently an idiopathic or toxic degeneration of the myocardium leading to heart failure.

Prognosis

During the past 50 years, the maternal mortality rate for the cardiac patient has declined markedly, mainly as the result of improved medical management (Table 3). Good medical management, in turn, implies a certain amount of patient cooperation as well as a willingness on the physician's part to hospitalize the patient at the first sign of decompensation.

Increasing age in the rheumatic subject is accompanied by an increased incidence of heart failure. Generally, the pregnant cardiac patient who is more than 25 years old should be seen weekly, regardless of functional status. There are no definite data thus far which show that increasing parity is accompanied by an increased rate of heart failure. Gorenberg and Chesley,¹⁹ in their report on the long-range prognosis in severe rheumatics, found no evidence that later pregnancies increased the average annual death rate.

A history of congestive heart failure, particularly if the failure occurred during a pregnancy, forewarns the physician of heart failure in the present pregnancy. With strict medical management these patients frequently can be carried through their pregnancy without heart failure occurring.

Chronic atrial fibrillation, although rare in the woman of childbearing age, is a serious finding. It indicates rather severe

organic heart disease and predisposes the patient to congestive failure as well as embolic phenomena. Mendelson,⁶ in a collected series, reported a maternal mortality rate of 12% and a fetal mortality rate of 50%.

Functional classification assigned prior to pregnancy can give an important estimate of the patient's ability to go through pregnancy. Class I and II patients generally have a minimum of trouble, but class III and IV patients account for almost all the cases of congestive failure and death⁶ (Table 4).

Generally, the chances of fetal mortality are increased in women with heart disease that is severe enough to produce symptoms; the more severe the disease, the greater is the possibility of fetal mortality. Burwell and Metcalfe⁵ have reported a fetal mortality rate of 8% for class III patients and 21% for class IV patients; these figures exclude therapeutic abortions. The maternal factors associated with increased fetal loss include severe congestive heart failure, severe congenital heart defects, and chronic atrial fibrillation as well as serious underlying medical or obstetric complications or both.

Summary

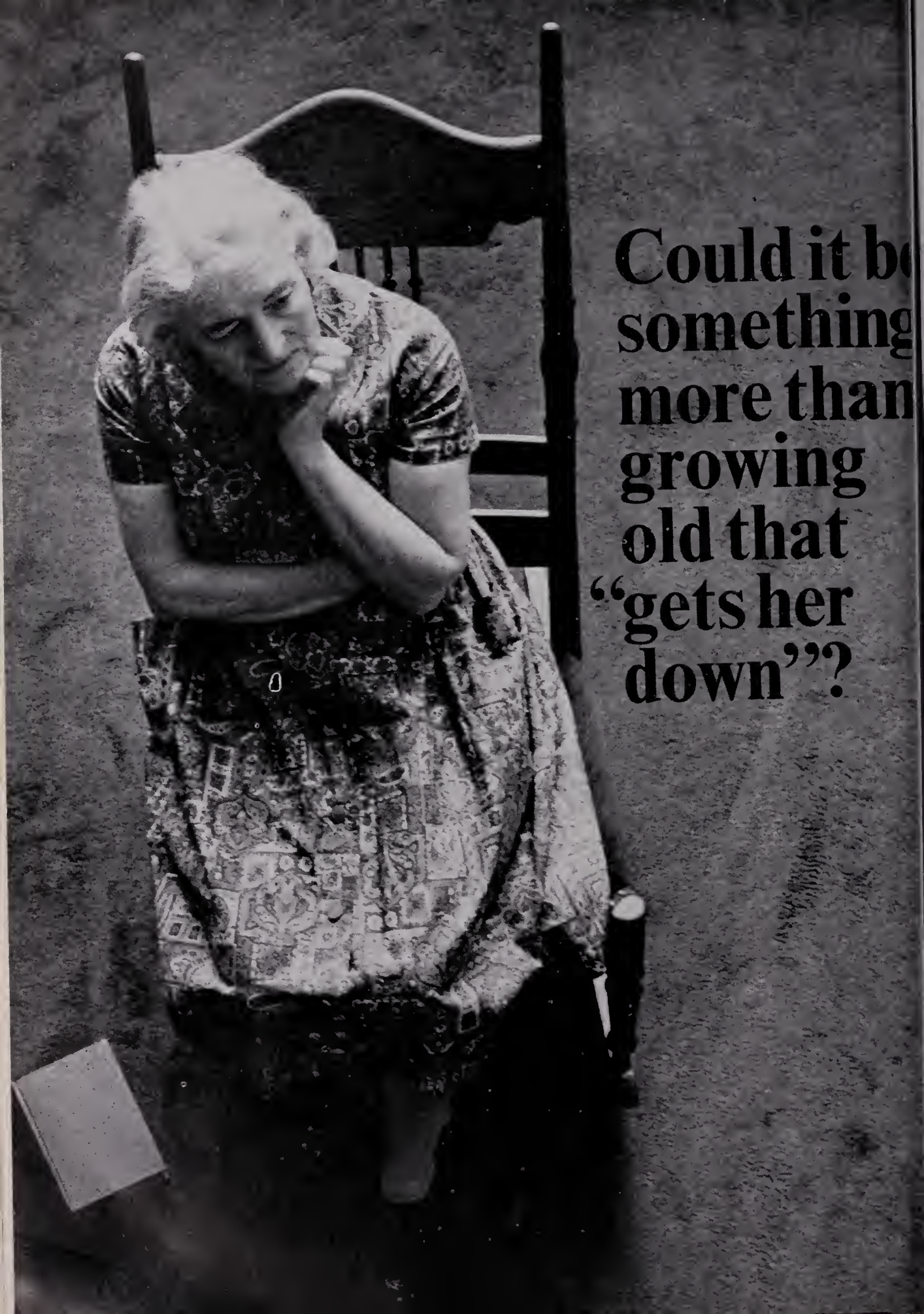
Heart disease may be associated in approximately 3% of all pregnancies. Evaluation and management are based on an understanding of the normal physiologic changes of pregnancy. Although heart surgery or therapeutic abortion may be performed, most of these patients can be successfully guided through their pregnancy, labor, and postpartum period by careful medical management based on the prevention and treatment of congestive failure. The maternal mortality rate is low (1½ to 1%), and death occurs almost exclusively in classes III and IV.

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References

1. New York Heart Association: Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Blood Vessels by The Criteria Committee. Ed. 5, New York, New York Heart Association, Inc., 359 pp. 1953.
2. Fitzgerald, J. E., Webster, Augusta, and Zummo, B. P.: Evaluation of Adequate Antepartum Care for the Cardiac Patient. JAMA 146:910, 1951.
- 3-29 May be secured from the author or the reprints.



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*Multiple of adult Minimum Daily Requirement supplied.

†The need for these substances in human nutrition has not been established.

Indications: 1. Functional fatigue such as that often associated with: a depressing experience or stressful time of life; advancing years; convalescence; limited activity or confinement. 2. Poor appetite and vitamin-mineral deficiency as they occur in: patients having faulty eating habits; geriatric patients who are losing interest in food; patients convalescing from debilitating illness or surgery.

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*15 mg. of Butisol (butabarbital), plus the other ingredients, in outer layer; 15 mg. of Butisol (butabarbital) in a specially coated core for delayed action, to approximately equalize duration of action for all components.

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uricemia and gout, bradycardia, drowsiness, skin rashes, hangover, systemic disturbances, weakness, leg cramps, diarrhea, epistaxis, dizziness, urticaria, dry itching skin, nausea, vomiting, palpitation, superficial skin bruises, headache, dehydration, paresthesias, photosensitivity, pancreatitis, jaundice, xanthopsia, thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, nasal congestion, hypotension, lassitude, loose stools, anorexia, bizarre dreams, peptic ulcer, ulcerative colitis, mental depression. (Ammonium chloride, which may be administered to reverse hypochloremic alkalosis, should not be given to patients with hepatic disease.) **Before prescribing or administering, see package insert.** †Warning: May be habit forming. **Usual Adult Dosage:** Butiserpazide®-25 or Butiserpazide®-50: 1 tablet daily or b.i.d. **References:** 1. Johnson, H. J., Jr.: *Penna. M. J.*: 67:35, 1964. 2. Coodley, E. L.: *Curr. Ther. Res.* 4:460, 1962.

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Hystero-graphy

A New Aid in Diagnosis of Hydatidiform Mole

THE DIAGNOSIS of a hydatidiform mole prior to the actual passage of molar tissue remains a perplexing and often frustrating problem. Rapidly increasing uterine size, absence of the fetus on abdominal x-rays, markedly elevated chorionic gonadotropin titers, vaginal bleeding and premature symptoms of toxemia suggest the presence of this tumor.

The unobstructed passage of a probe through cervical canal well into the uterine cavity has been considered by many to be the ultimate definitive diagnostic procedure. The hazards of the "probe test" to a normal intrauterine pregnancy are obvious.

Torres and Pelegrena recently described transabdominal intrauterine contrast medium injection as a safe and accurate diagnostic technique. This procedure was used in evaluating the following patient.

Case Report

This 23-year-old white gravida II para I was first seen in the office October 18, 1966. Her last menstrual period had been August 18, 1966. She had delivered a full term male infant June 14, 1964. Physical examination was essentially normal. The uterus was approximately three times normal size. The microhematocrit was 40.

She first noted scanty, brown vaginal discharge October 25, 1966. One week later an episode of moderately profuse vaginal bleeding occurred. She was then hospitalized. Her uterus had now enlarged to a point midway between the pubis and the umbilicus. The cervix was thick and closed. No tissue had been passed. The hematocrit was 36. The chest x-ray was reported to be normal. A twenty-four-hour urine gonadotropin level was reported as "greater than 325,000 i.u. and less than 487,000 i.u./24 hours; in the high normal range." The patient was dismissed from the hospital and arrangements were made to see her frequently in the office.

Intermittent vaginal bleeding continued. On November 28, 1966, the uterus was enlarged to the level of the umbilicus. No fetal heart tones were heard. The microhematocrit was 33. Urinalysis revealed 1+ albuminuria. A probe was gently passed through the cervical canal to a depth of four inches without meeting resistance.

The patient was re-hospitalized. The following day her abdomen was surgically prepared and draped. The procedure was then monitored with image intensified fluoroscopy with the television projection. A scout film revealed no evidence of a fetus. Following local infiltration with 1% Carbocaine a No. 18 spinal needle was introduced transabdominally in the midline 3 to 5 cm. below the umbilicus into what was thought to be the uterine cavity. Aspiration was not productive of blood or amniotic fluid. Several cc. of a test dosage were injected, then rapidly 50 cc. of Hypaque. Fluoroscopy revealed the typical "moth-eaten or honey-combed pattern (See Figures 1 and 2) considered to be unquestionable radiographic evidence of a hydatidiform mole."

Continued



Figure 1



Figure 2

The injection was repeated in approximately thirty minutes because we were not prepared for the almost instantaneous absorption and renal excretion of the dye. The characteristic pattern again appeared.

That evening the patient spontaneously passed 545 grams of clots and typical grape-like molar tissue. A dilation and curettage were done the next morning, with removal of more molar tissue. Prior to hospital discharge the patient was given a prescription for an ovulation-inhibiting drug. Pregnancy tests during the subsequent two weeks have been negative.

Summary

The described technique proved to be therapeutic as well as diagnostic in this case. It is the author's cautious impression that perhaps the hystero-gram, using proper precautions including the injection of a maximum of 50 cc. of opaque material, is less hazardous and more illuminating than the "probe" test in the diagnosis of a hydatidiform mole.

Joseph S. Massee, M.D.
Minneapolis, Minnesota

Reference

1. Torres, A. H., Pelegrina, I. A.: *Amer J Obstet Gynec* 94:936, 1966.

For Smallpox

A medical student, Thomas Dover, residing in Thomas Sydenham's house, had the smallpox — and later he told how the master treated him: 'First I was bled to the extent of twenty-two ounces; then an emetic. I had no fire allowed in my room, my windows were constantly open, my bed-clothes were ordered to be laid no higher than my waist. He made me take twelve bottles of small beer, acidulated with spirit of vitriol, every twenty-four hours.'*

*Massengill, S. E., M.D.: *Sketch of Medicine and Pharmacy*. S. E. Massengill Co., Bristol, Tenn.-Va., ca. p. 56, 1941.

The Physician's Workshop

Needle Biopsy

Use of the Schleicher Tissue Core Instrument

THE SCHLEICHER TISSUE Core Instrument,¹ originally designed for bone marrow biopsy, is a practical tool for obtaining undistorted tissue from other organs. The commonly used biopsy instruments may tear, compress, or break up the specimen because suction has to be applied to sever the tissue from the organ. These artefacts* make it difficult to evaluate the histology. In addition, the instruments are complicated, easily damaged, and costly. The Schleicher tissue core instrument is well designed, sturdy, inexpensive, and easy to use.

The Instrument

The Schleicher tissue core instrument is available in four gauges: 13, 15, 17, and 19. The total length of the instrument with the core shaft hub attached is 13 cm. The core shaft measures 11.5 cm.** and has a conical razor-sharp bevel that cuts smoothly through soft tissue. Situated above the bevel is a 1-cm. straight slot and an air hole. A pointed stylet and a flat end obturator complete the unit. The instrument is shown in Figure 1. (See next page.)

Technique

The skin is sterilized and anesthetized. A small incision is made into the skin over the organ to be biopsied. The cutting edge of the core shaft bevel is lined up with the base of the stylet point. The core shaft is tightly secured in the hub by the set screw. The instrument is held as shown in Figure 2 (next page). The core shaft with the stylet in place is advanced through the incision into the organ, penetrating it for a distance of one to two millimeters. The stylet is then withdrawn. Slight pressure is applied while slowly rotating the instrument clockwise. When a core of about 3 to 4 mm. has been cut, a slight resistance is felt. If a longer specimen is wanted pressure is increased.

Severing the Tissue Core

Before withdrawing the instrument, the bevel is moved about 1 mm. up, down, or sideways in order to sever the core from the organ. The instrument is now rapidly rotated several times and withdrawn. The straight slot allows inspection of the specimen. Tissue cores of 1 cm. are readily obtained without distortion of the histology.

Expelling the Core

A solid tissue core can be expelled immediately with the flat end ob-

Continued

*See Test Your Word Score Page 687.

**Core shafts of any length and the instrument can be obtained from the manufacturer Becton, Dickinson and Company, Rutherford, New Jersey 07070.

turator. To prevent the core from bulging into the slot opening, a finger or a transparent plastic tubing is placed over the slot. The specimen is immediately immersed in formol-saline fixing fluid* (See footnote at bottom of next page) and allowed to harden for one hour.

If the core is too fragile to expel, the specimen is left in the shaft, which is disengaged from the hub by loosening the set screw. The shaft is placed in the fixing fluid for one hour. The slot and the air hole permit the fluid to come in contact with the tissue core. The tissue core

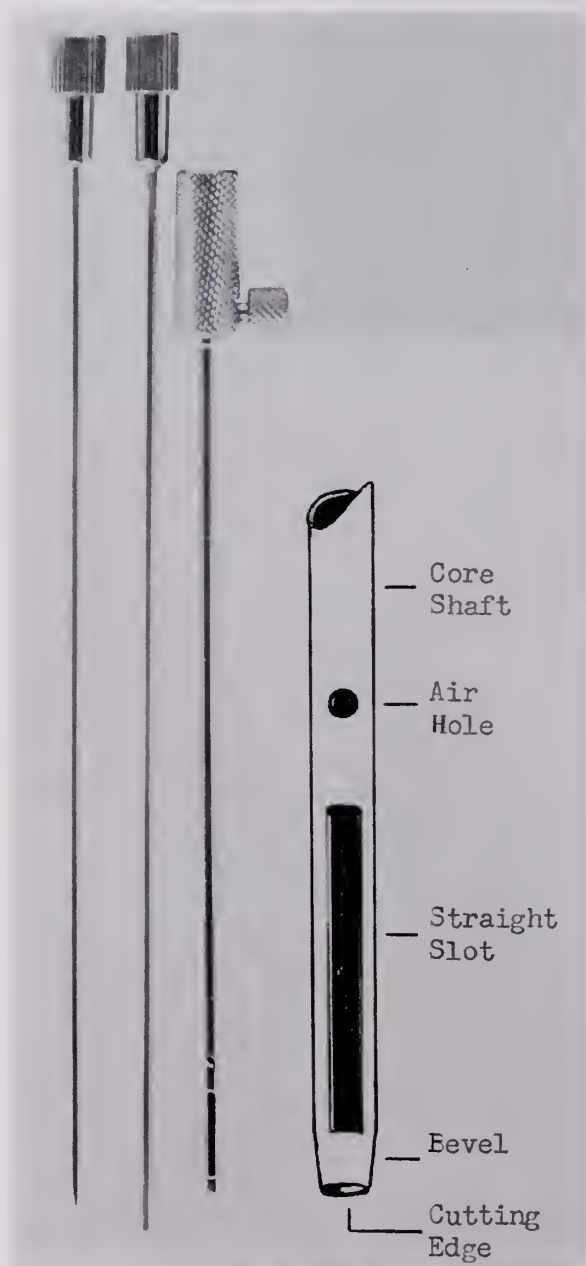


Fig. 1 — Schleicher Tissue Core Instrument. Left to right: pointed stylet, flat end obturator, core shaft with detachable core shaft hub and set screw. Drawing shows the bevel, cutting edge, straight slot, and air hole of the core shaft.

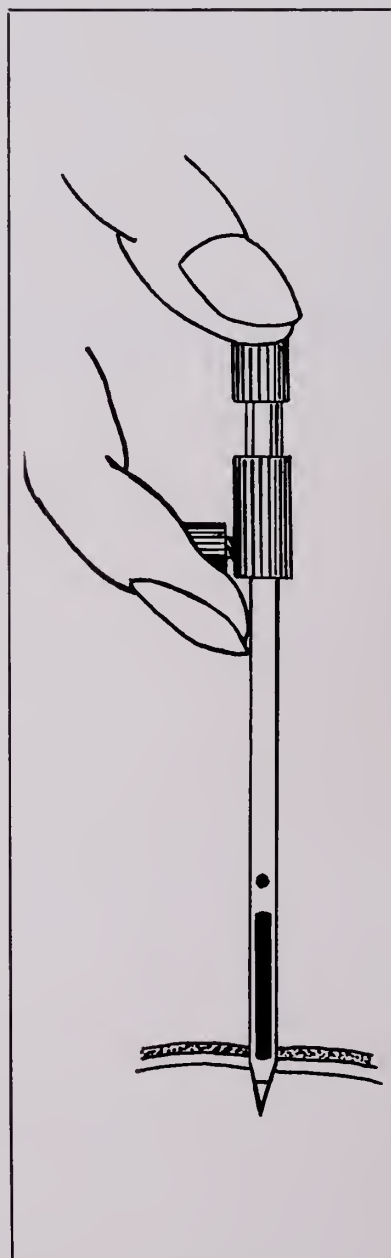


Fig. 2 — The assembled Schleicher Tissue Core Instrument in situ. The pointed stylet is withdrawn when the organ has penetrated about one to two millimeters.

NEEDLE BIOPSY

contracts slightly with fixation and can be readily expelled for further hardening.

Processing the Core

If a core contains calcium, the specimen is placed, after the initial fixation, into a decalcifying solution** for one-half to one hour. It is washed in tap water for a few minutes and placed in 80 per cent alcohol until ready for processing. A properly fixed and decalcified tissue core can be handled routinely in the histology laboratory.

When a tissue core is taken during surgery the bevel of the core shaft without the stylet is placed directly on the surface of the organ and the specimen obtained as described above.

Testing the Core Shaft Bevel

The razor sharpness of the core shaft bevel can be tested by rotating and slightly pressing the cutting edge against a few layers of cleansing

*Fixing Solution	
Neutral Formaldehyde 40%	10 ml.
Physiologic Sodium Chloride Solution	90 ml.
**Decalcifying Solution	
Distilled Water	800 ml.
Formaldehyde 40%	80 ml.
Conc. Nitric acid	40 ml.

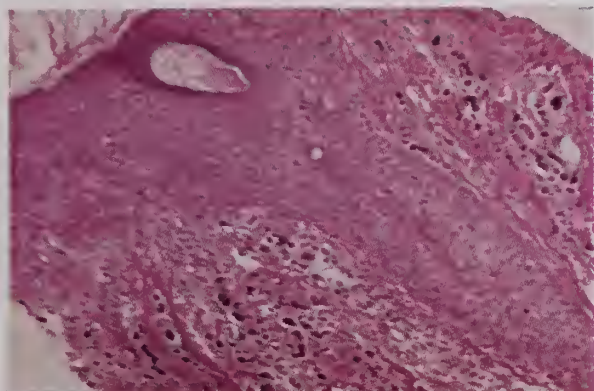


Fig. 3 — Core biopsy of skin nodule. Schleicher tissue core instrument 15-gauge. Hematoxylin-Eosin, $\times 125$.

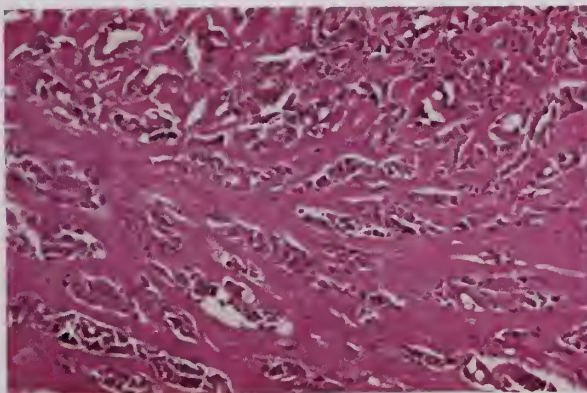


Fig. 4 — Core biopsy of breast. Schleicher tissue core instrument 13-gauge. Hematoxylin-Eosin, $\times 500$.

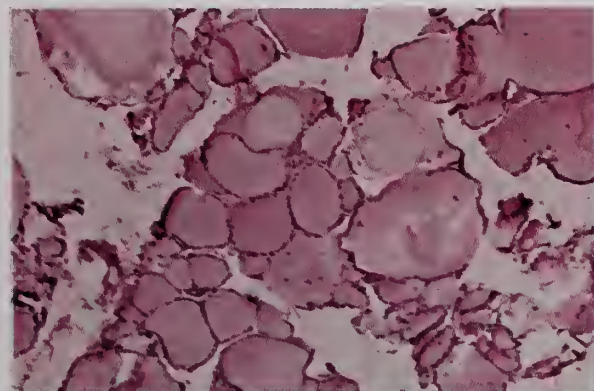


Fig. 5 — Core biopsy of thyroid. Schleicher tissue core instrument 15-gauge. Hematoxylin-Eosin, $\times 125$.

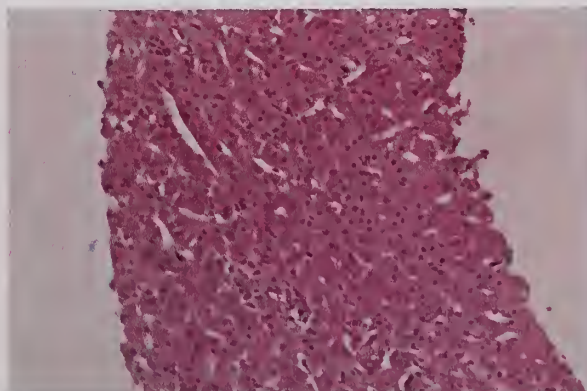


Fig. 6 — Core biopsy of liver. Schleicher tissue core instrument 15-gauge. Hematoxylin-Eosin, $\times 50$.

Continued

paper. A sharp edge readily cuts smooth-bordered discs which are retained in the lumen of the core shaft. Sharpness of the cutting edge is restored by moving the bevel across a No. 000 emery paper.

Comments

Using the procedure as outlined we have procured forty-five tissue cores from various organs with the Schleicher tissue core instrument. All specimens have been of good quality. Biopsy sites include breast, liver, thyroid, lymph nodes, and skin. Figures 3, 5, and 6 show core histologic preparations of a skin nodule, thyroid, and liver obtained with the 15-gauge, and Figure 4 of a breast biopsy procured with the 13-gauge instrument. The 13-gauge core shaft is preferred by us for breast biopsy and for tissue cores taken during surgery. Diagnostic specimens have been obtained, however, with the 15, 17, and 19-gauge instrument.

Summary

The Schleicher tissue core instrument is ideally suited for obtaining a specimen for biopsy from soft organs other than the bone marrow. The technique is described.

The tissue core cut by the razor-sharp bevel preserves the architecture of the tissue. Because the specimen may be fixed within the lumen of the core shaft, artefacts are minimal. Forty-five tissue cores have been procured from various organs; all specimens have been of good quality.

Acknowledgement

Thanks are extended to Dr. W. A. Chadbourn and Dr. R. L. Reece, Department of Pathology, St. Barnabas Hospital, and Dr. A. R. Jay, Department of Pathology, The Swedish Hospital for their evaluation of the tissue cores, and to Dr. E. M. Schleicher for his technical assistance.

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Reference

1. Schleicher, E. M.: A New Instrument for Obtaining Bone Marrow for Biopsy. Minnesota Med 49:1319, 1966.

Perfection

There are some who are so beautiful that disease cannot deform them, and who are endowed with such exquisite life that they would turn to smile back on you over the brink of the grave. — George Moore

Your Age

The old believe everything; the middle-aged suspect everything; the young know everything. — Wilde

Vesicoureteral Reflux in Children*

A Brief Review

THIS IS INTENDED to be an impartial review rather than a defense of a particular thesis. It is based upon personal experience, observation, and rather wide reading.

The Ureterovesical Junction

It has been demonstrated conclusively by many observers that passage of urine up the ureters is an abnormal phenomenon in man. It is said to be prevented by the obliquity of the intramural and particularly of the submucosal ureter (Figure 1). The latter is compressed as the intravesical pressure rises during urination. Since the trigone contracts during urination to pull open the internal meatus, Hutch believes that this same contraction also lengthens and flattens the submucosal ureter, thus supplementing the antireflux effect of the intravesical pressure. Normal ureteral peristalsis also exerts a protective action, as evidenced by Figure 2. This urogram was made 12 years after a Boari operation, which involves no attempt to mimic the ureterovesical valve.

The Deleterious Effects of Reflux

Vesicoureteral reflux can injure the upper urinary tract in four ways: (1) It subjects the ureters and kidneys to the voiding pressure, which greatly exceeds that normally prevailing in the ureters and kidneys. If unchecked, this leads to dilatation and later thinning, at first of the ureters and later of the renal pelves, finally with hydronephrotic atrophy and impaired renal function. Any obstruction to urination aggravates these effects by raising the voiding pressure. (2) Any increase in the ureteral lumen di-

minishes the effectiveness of peristalsis, and thinning of the ureteral wall reduces its force, thus enhancing the untoward consequences of reflux by inducing secondary stasis of urine. (3) Bacteria in the bladder may be propelled to the kidneys. (4) Much of the regurgitated urine descends to the bladder immediately after voiding has reduced the intravesical pressure, so that there is residual urine whether there is obstruction to urination or not. This defeats the "washing effect" of micturition which Cox and Hinman believe to be essential in eliminating bacteria from the bladder.

Historical Highlights

Although Hutch in 1952 was apparently the first to try to eliminate existing reflux surgically, its occurrence and most of its causes had been known for a great many years. The attitude of urologists toward reflux before 1952 suggests Mark Twain's remark about the weather — "everyone talks about it, but no one does anything about it." Galen (about 150 A.D.) is said to have found that he could not squeeze urine from the dog's bladder into his ureters (Polk). DaVinci sketched the oblique course of the ureters through the vesical wall in the 15th century (Belt). Zemblinoff in 1883 observed reflux in the anesthetized rabbit, an observation verified in 1893 by Lewin and Goldschmidt, who also commented that the phenomenon was rare in the dog because his bladder was thicker and his ureterovesical junctions more oblique than those of the rabbit. Harrison had already (1884) declared that reflux in man was abnormal because of this obliquity.

The disorder has been produced experi-

Continued

*Based upon a paper given before the South Central Section of the American Urological Association at Mexico City in October, 1966.

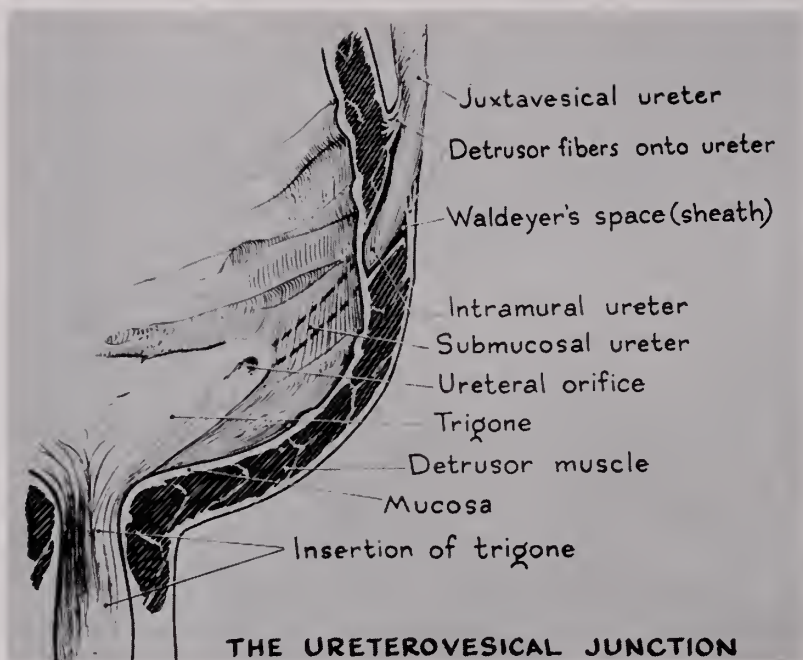


Fig. 1 — The bladder and ureterovesical junction.

mentally by slitting the roof of the submucosal and intramural ureters (Andler 1925 and Gruber 1929); by lumbar sympathectomy (Tanagho and Hutch); by pelvic neurectomy (Torbey and Leadbetter); by cross cutting the trigone just below the ureteral orifice (Hutch); and by implanting pellets of sterile paraffin into the bladder and later infecting them (Sommer and Roberts).

Kelly in 1899 had seen air bubbles issue from the ureters during air endoscopy; Alksne (1908) had a patient void through a post nephrectomy ureteral stump. In 1924 Bumpus found reflux in 8.6 per cent of 1036 cystograms, chiefly in adults, and attributed it to infection, including tuberculosis, to neurogenic vesical dysfunction, and to operations upon the bladder. Schmidt (1927) stated that irritating contrast agents could cause it, and a year later Blum spoke of "anomalies of the valves." Brattstrom found a straw in the renal pelvis, while others reported such oddments as a toothpick in an ureteral stone and a hairpin in a renal calculus.

The experimental production of reflux by slitting the submucosal ureter has its counterpart in man in ureteral meatotomy for stone and ureterocele, and in nonoblique re-

implantation of the traumatized ureter.

Common Causes of Reflux in Children

To simplify this presentation I am eliminating reflux due to prostatism, to neuro-



Fig. 2 — Urogram 12 years after a Boari operation, which substitutes a tube of vesical wall for the distal ureter.

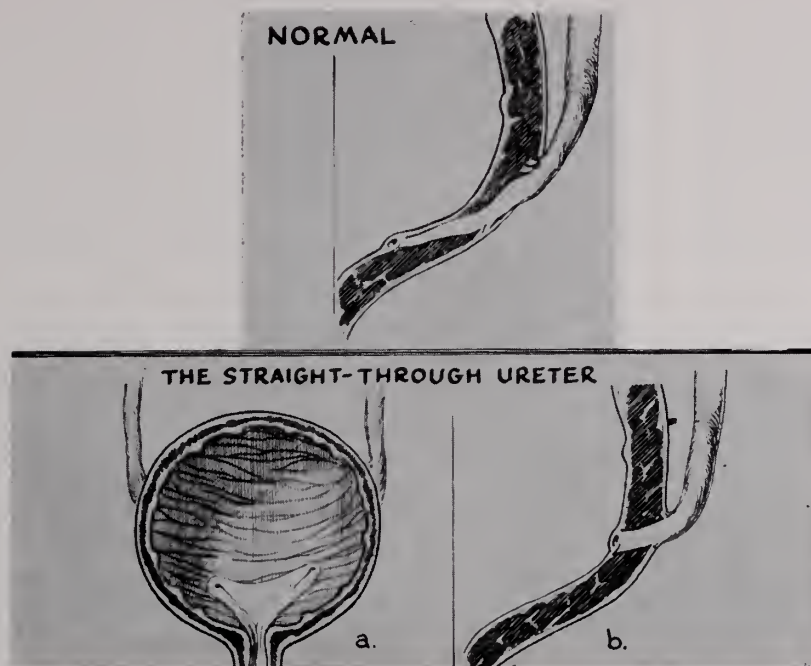


Fig. 3 — The “straight through” compared to the normal terminal ureter.

genic vesical dysfunction, to tuberculosis, and to operations. Within these limitations the commonest cause in children appears to be a localized anomaly in which the ureter passes straight through the vesical wall (Figure 3). It may be unilateral or bilateral and may occur without any other anomaly. It has also been attributed to a “weak trigone,” to some abnormality of Waldeyer’s sheath (Figure 1) and, of course, to the thin-walled bladder of the megacystis syndrome. Reflux occurs both with and without obstruction to urination, which probably serves to aggravate rather than to cause the disorder, unless protracted and severe.

This applies also to valves of the posterior urethra and to such other obstructive lesions in the male as interfere only *mildly* with urination. However, the more severe and long standing lesions probably both initiate reflux by thinning the detrusor and aggravate its effects by increasing the voiding pressure.

One can only speculate on the role of infection in causing reflux in children; in most instances it is probably a complication rather than a cause, although Hutch and others have shown that it may accompany acute cystitis in the adult female, and disappear with its subsidence.

The Clinical Picture

The disorder most often manifests itself as recurrent or chronic urinary infection; reflux should also be considered in children with symptoms of obstruction to urination.



Fig. 4 — Slight dilatation of terminal ureters suggesting (but not proving) presence of reflux.

Continued

Renal pain during or after urination is uncommon. Markland has pointed out that reflux may remain asymptomatic until renal failure from hydronephrotic atrophy appears in later life.

Recognition

The excretory urogram may be normal but will often disclose some dilatation of the pelvic ureters (Figure 4). Ureteropyelectasis is always suggestive. It is feasible, but tedious, actually to demonstrate reflux in the urogram if stasis is not too severe. After a late film has shown the upper tract fairly empty, another is exposed after appearance of the desire to void, and a last one during micturition (Figure 5). Refilling and dilatation of the upper tract are diagnostic.

Cystourethrography

We ordinarily expose a large film after filling the bladder to the point of tolerance,

*The patient voids into a metal container with the microphone of a tape recorder attached. One thus gets information about the force of the stream, intermittency, and volume voided per second.

a second one during micturition, and a third one just afterward. I have learned not to lean too heavily upon the configuration of the urethra, since psychic inhibition may make it look small, and the internal meatus spastic, when both are actually normal. Conversely, one may find at operation a rigid internal meatus which looked normal in the urethrogram. Valves of the prostatic urethra are, of course, readily identified (Figure 6).

Cine

Cine cystourethrograms have the advantage of showing (sometimes) ureteral peristalsis as well as the behavior of the bladder and urethra — if well done. The longer period of observation increases the chances of observing fleeting reflux; but is such reflux important?

I believe that the "piddle pattern"* of Lyon and Smith is a better guide to the adequacy of the bladder and of its outlet than is either of the preceding methods, but one must put everything together.



Fig. 5 — Demonstration of reflux during excretory urography. (a-left) Twenty minute film; (b-right) Voiding film showing refilling and distention of upper tract.

Cystoscopy

At *cystoscopy* one calibrates the female urethra with olivary bougies with a view to correcting any distal narrowing; these bougies are too traumatic in the male. Visual observation is a poor guide to minor abnormalities around the internal meatus in the female, so much so that I wonder whether the "weak trigone," which Hutch regards as important in the production of reflux, may not also impede normal micturition. It is generally accepted that contraction of the trigone pulls open the internal urinary meatus; if this action is incomplete or defective, it seems likely that micturition will require an abnormally high pressure with a small stream. It requires alertness and experience to recognize those valves of the posterior urethra which are inframontane.

Absence of trabeculation suggests absence of outlet obstruction. False trabeculation can be produced by deliberate overdilatation of the bladder under anesthesia. One sees gaping ureteral orifices without demonstrable reflux and submucosal ureters of appar-

ently normal length with total reflux.

Hutch and others have observed that the trigone is likely to be wider than normal in the refluxing patient. Cystoscopic findings may be inconclusive or misleading; this examination should always be supplemented by cystourethrography if reflux is suspected.

Both Amar and Matzkin have demonstrated reflux cystoscopically by first distending the bladder with a solution of indigocarmine, draining it, and then watching the ureteral orifices. Blue spurts therefrom are diagnostic but are not an index of the severity of ureteral or renal damage.

A Simplified Clinical Classification

I. All may be unilateral or bilateral, and with or without ureteral duplication or obstruction to urination.

II. Fleeting

A. Incomplete

B. Total

III. Persistent complete

A. With normal upper urinary tract

B. With moderate dilatation

C. With severe dilatation and impaired renal function

Treatment

While opinions vary as to what should be done about reflux, it is agreed that any obstruction at the vesical outlet must be eliminated to minimize voiding pressures. Beyond that, views can be classified as follows:

Reflux

Never operate upon the ureters for reflux, but limit treatment to:

1. Training

a. Correct wiping

b. "Gentle" urination

c. Timed and double or triple voiding (What of untrained infants and of resistive teen-agers?)

2. Urethral dilatation, including avulsion of "distal urethral stenosis."

3. Meatotomy, urethrotomy

Plastic Operation

Always perform a plastic operation on the vesical neck with or without preliminaries. Both groups count on "maturation" of the

Continued



Fig. 6 — Reflux secondary to valves of posterior urethra. There is none into the upper segment on the right.



Fig. 7 — Reflux with intact upper urinary tract.



Fig. 8 — Reflux with definite dilatation of ureters and pelves.

bladder to thicken it and so to eliminate reflux (Hutch, Baker et al., King).

Vesicoureteroplasty

Always use vesicoureteroplasty, usually with a Y-V plasty or equivalent, if reflux can be demonstrated.

There is obviously room for the application of each of these methods. One should fit the treatment to the patient's problem rather than the reverse.

The Author's Views

For fleeting reflux, or for total reflux with little or no ureteral dilatation (Figure 7), correct any obstruction to urination, short of a plastic at the internal meatus; I believe that, if the bladder is to be opened, vesicoureteroplasty should be considered. Timed voiding and prolonged suitable antibacterial therapy are then instituted, together with close follow-up. If the mother is not intelligent, conscientious, and persistent, or if the child is too young to cooperate or is a rebellious teen-ager, this regimen will probably fail.

A conscientious follow-up is essential. It



Fig. 9 — A degree of hydronephrosis requiring preliminary nephrostomy.

includes periodic microscopic examination and cultures of clean voided urines, measurements of renal function for comparison, cystograms and urograms, bearing in mind the perils of over-irradiation.

If the conservative regimen fails, vesico-ureteroplasty, with or without Y-V plasty, should be considered.

If there is moderate dilatation with good renal function (Figure 8), treatment should be surgical, as just outlined.

If ureteropelvic dilatation is advanced

with definite impairment of renal function (Figure 9), preliminary nephrostomy is done; some will prefer cystostomy, which I dislike. If renal and ureteral function (cinefluoroscopy for the latter) improve, the ureters are narrowed, perhaps shortened and reimplanted, and the internal meatus is widened.

Should renal function fail to improve and the ureters remain inert, the next step is pyeloileoplasty, although there is a place, despite some impairment of peristalsis in

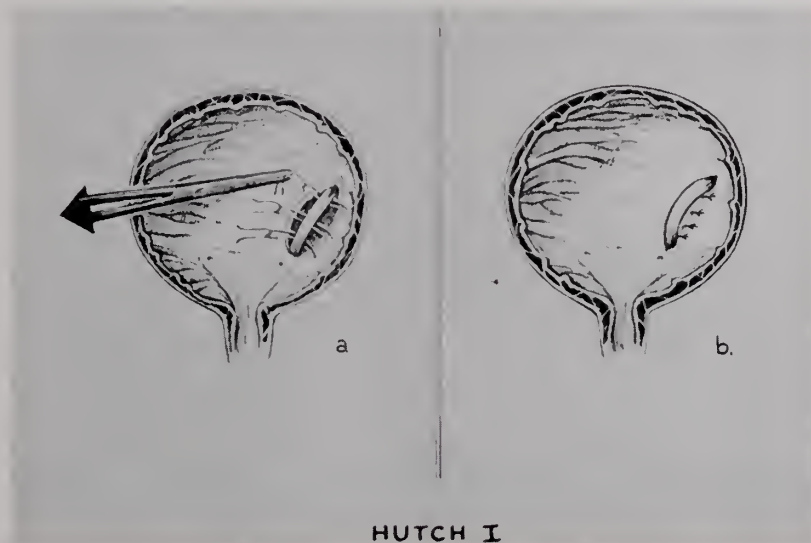


Fig. 10 — The Hutch operation.

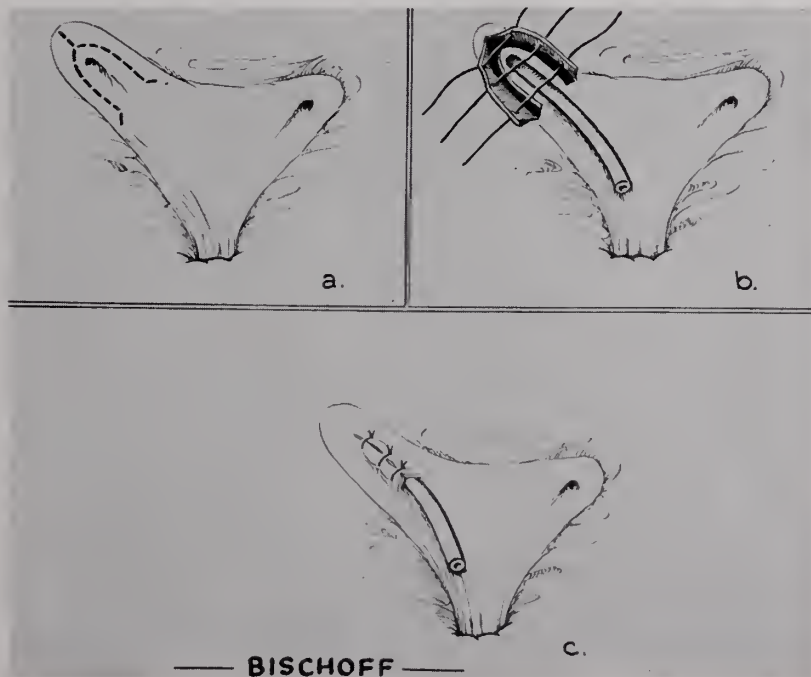


Fig. 11 — Bischoff's method.

Continued

relatively thick walled ureters, for tubeless cutaneous ureterostomy with wide uretero-ureterostomy where the ureters pass through the abdominal wall. I have been disappointed with tubeless cystostomy.

Types of Vesicoureteroplasty

The Hutch Operation

First in point of time is the operation

of Hutch, designed originally to stop reflux in paraplegics (Figure 10). However, experience has shown that the principle of leaving a bare ureteral segment within the vesical lumen to be covered by mucosal proliferation is wrong, since scar often constricts the ureter as it enters the lumen of the bladder.

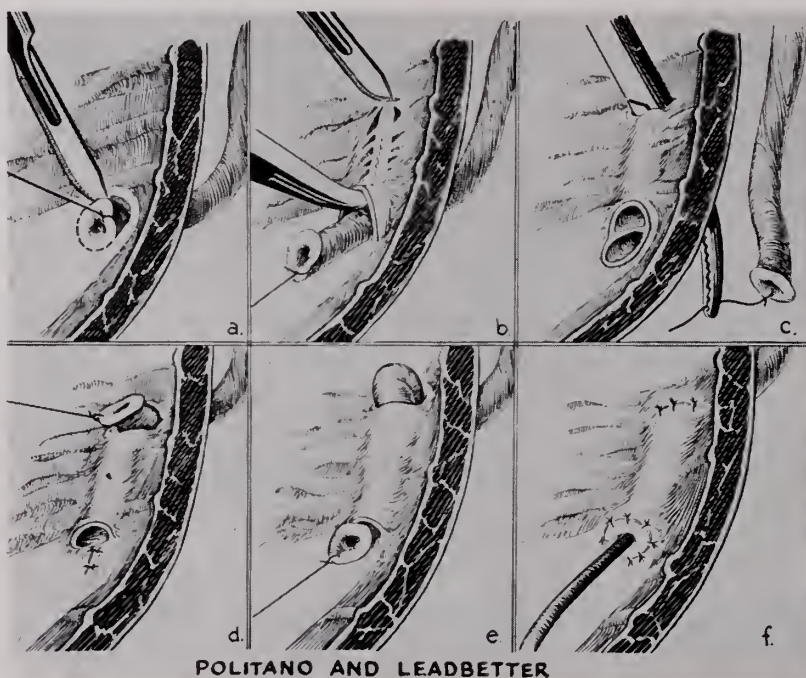


Fig. 12 — Technique of Politano and Leadbetter.

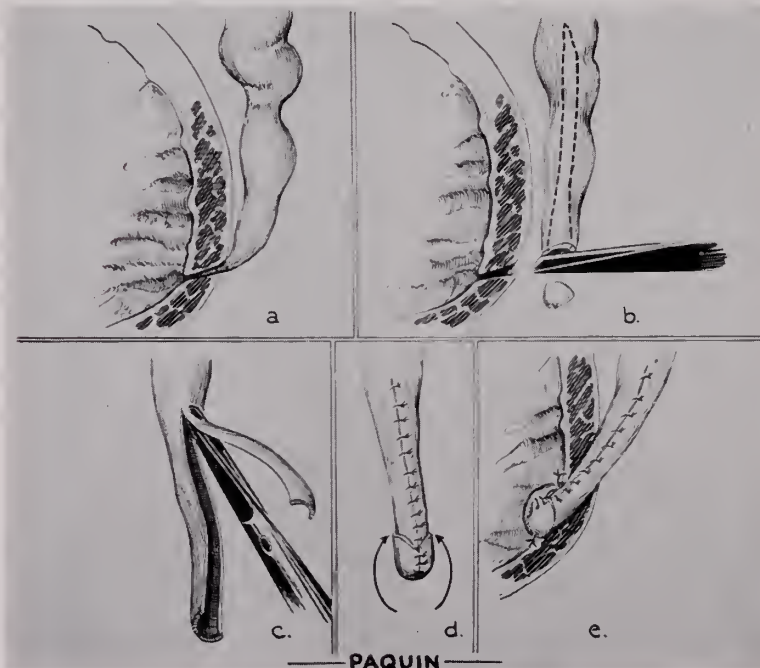


Fig. 13 — Paquin's operation.

Bischoff's Operation

The virtue of *Bischoff's* operation (1957 — Figure 11) is that it is unlikely to do any harm. However, it requires a considerable distance between ureteral orifices and internal meatus, and a large bladder; data concerning results are meager.

Politano and Leadbetter

The method of *Politano* and *Leadbetter* (1958 — Figure 12) has been most widely used and has yielded a high proportion of successes. It can be applied to any type of ureter. However, if dissection has to be carried high onto the ureter, there is some

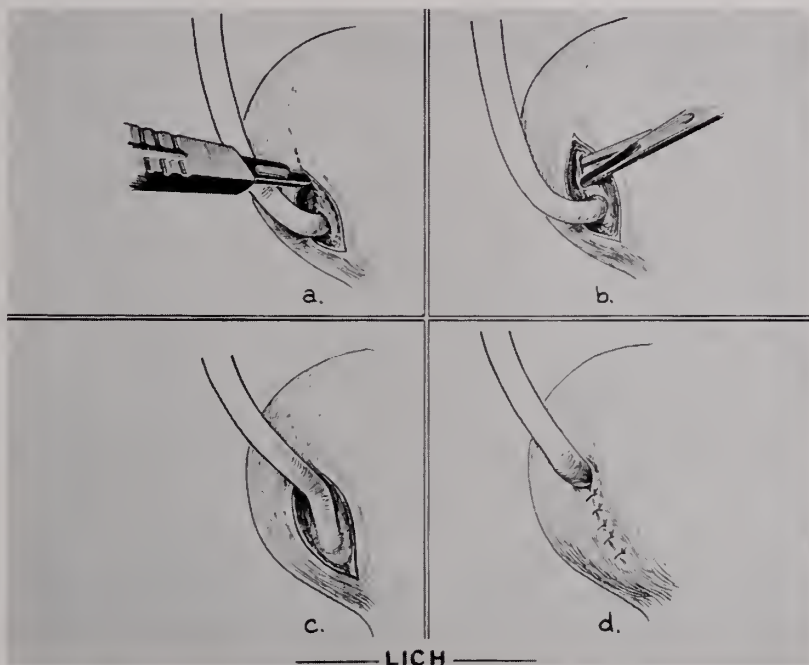


Fig. 14 — Lich's method.

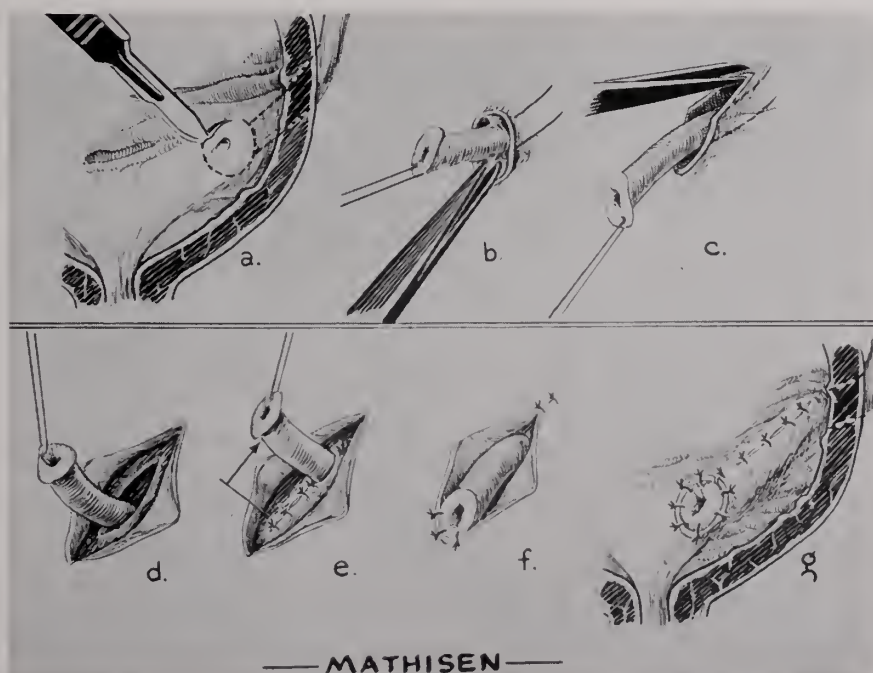


Fig. 15 — Mathisen's modification of the Politano-Leadbetter operation.

Continued

danger of injury to intraperitoneal structures so that, if one has to narrow or excise much of the ureter, it should be exposed extravesically.

Other Procedures

In 1959 *Paquin* (Figure 13) devised a method combining an ureteral cuff with oblique submucosal implantation; the operation is useable for any kind of ureter.

Lich's operation (1961) is made clear by Figure 14.

Mathisen's procedure (1964 — Figure 15) is essentially that of Politano and Leadbetter except that the ureter is buried in a trough instead of a tunnel.

The various techniques of ureteral advancement (Hutch, Williams, Witherington, Edelbrock), of which Figure 16 is an example, all require a reasonable distance from ureteral orifice to internal meatus.

Results of Treatment

It is difficult to assess these accurately from the literature. Some speak of the number of ureters, others of the number of patients; often the length of the follow-up is not mentioned. At other times it is hard to say whether the patients had only Y-V plasty of the vesical neck, or whether the

ureters were also reimplanted. In other instances reported series are too small for worthwhile evaluation. It is, for these reasons, often impractical to combine series in order to assess larger numbers.

Conservative Treatment

Stephens in 1962 reported on 34 patients observed for five to 10 years during and after protracted antibacterial therapy and "multiple micturition." Forty of 59 ureters (67.7 per cent) were still refluxing, a situation which he regards as of no importance as long as infection does not occur.

Leuzinger et al. in 1959 regarded 30 of 44 patients treated conservatively for an unstated period as "improved," a statement too vague for analysis. This left 32 per cent unimproved and presumably refluxing.

Melick and associates (1966) found, after a followup of one or more years of conservative therapy, that 56 per cent still had reflux.

King has stated that antibacterial therapy and multiple micturition will result in disappearance of reflux in three fourths of patients in whom the disorder is uncomplicated, i.e., no outlet obstruction, neurogenic dysfunction, etc. However, he has presented no specific data.

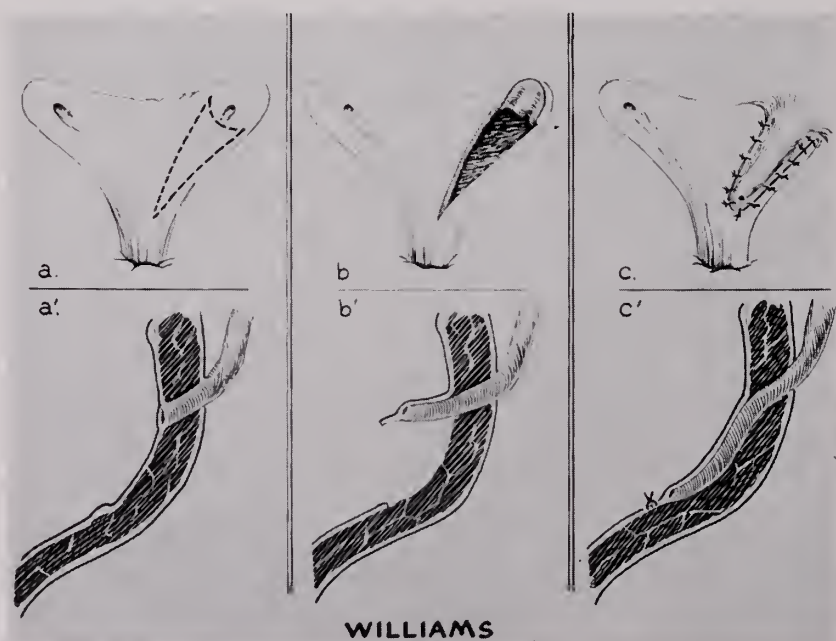


Fig. 16 — William's ureteral advancement.

Plastic Operations on the Vesical Neck

One can, for this purpose, combine the results of the various plastics with those of transurethral resection. The series of Pasquier et al., the Leadbetter, Melick et al., and Harper and Politano add up to 106 patients, of whom 60, or 56 per cent, still had reflux at an unstated time after operation.

Vesicoureteroplasty

The operation of Politano and Leadbetter has been most consistently successful. Politano followed 100 patients for five years; Scott reported on 66 ureters, and Williams on 57 patients: a total of 217 instances, with reflux persisting in eight or 3.7 per cent.

McGovern has summarized the results of the Paquin operation in 327 ureters in 226 patients followed for an average of 4.5 years. Reflux was still present in 10 per cent.

In the case of Mathisen's method, he saw reflux persist in 10 of 44 patients, while Bettex saw it in 18 of 101 ureters, a combined failure rate of 19 per cent.

In regard to Hutch's operation, only small series have been reported. Combining the series of Pasquier et al., Fuqua and associates, Johnston, Williams and Eckstein, and Ambrose and Nicholson, we find that reflux persisted in 24 of 121 patients, or 20 per cent. One must bear in mind Hutch's own statement that this operation is too often followed by stricture where the ureter enters the vesical lumen.

Causes of Failure

Since this presentation is not concerned with surgical technique, causes of failure of vesicoureteroplasty are merely summarized. They appear to result largely from errors of judgment and of technique. Included are reimplantation of ureters which are too large, or of those in which peristalsis is inadequate. Also operative are constriction at the site of reimplantation and unduly sharp angulation of the ureter.

Comments and Conclusions

The phenomenon of vesicoureteral reflux has been known and studied for at least 125 years, during which time it has become

firmly established as abnormal in mankind. During this period its causes (local anomalies, urinary infection, obstruction at the vesical outlet, neurogenic vesical dysfunction, thin-walled bladders, and operations upon the ureterovesical junction) have become well known. Its deleterious effects upon the urinary tract are also well understood and have ample experimental confirmation. However, deliberate attempts to correct it surgically date back only about 15 years, although plans to prevent it by oblique submucosal reimplantation of the injured ureter are much older.

The objective of treatment is to stop the noxious effects of reflux and to eliminate infection. While opinions differ sharply as to whether the definitive therapy should be medical or surgical, it is generally agreed that any vestige of obstruction to urination must be eliminated by whatever method required.

Beyond this, opinions are divided into two divergent groups: those who decry vesicoureteroplasty, and those who advocate it. The first group, maintaining that reflux per se is harmless, put their faith in a long time bacterial therapy and in timed, multiple micturition. A subgroup holds that the bladder may, as it matures, thicken and stop the reflux. Should this fail to occur, however, the patient will have to maintain constant vigilance throughout his life in order to protect his urinary tract. Experience with patients makes me doubt that many will do so over the long run, and there is acceptable evidence that many instances of terminal renal failure result from unrecognized, life-long reflux.

Since vesicoureteroplasty, particularly of the Politano-Leadbetter and Paquin types, has yielded good results in more than 90 per cent of suitable cases with a low incidence of complications, it seems sensible to say that, if a reasonable trial of closely supervised and conscientiously executed conservative therapy fails to eliminate the reflux, vesicoureteroplasty should be considered. There are, of course, situations in which the ureters gape, and total reflux

Continued

ADVANCES

occurs at low intravesical pressures and volumes, in which vesicoureteroplasty should receive first consideration. There are others

in which renal and ureteral damage is so far advanced that urinary diversion offers the only hope of halting renal destruction of the kidneys.

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References

1. Alksne, J.: A Contribution to the Normal and Pathologic Physiology of the Ureter. *Folia Urol* 1:338, 1907-1908.
 2. Amar, A. D.: Cystoscopic Demonstration of Vesicoureteral Reflux. *J Urol* 95:776, 1966.
 3. Ambrose, S. S., and Nicholson, W. P.: Vesicoureteral Reflux Secondary to Anomalies of the Ureterovesical Junction. *J Urol* 87:695, 1962.
 4. Andler, A.: Contribution to the Etiology and Clinical Nature of Vesicoureteral Reflux. *Mitt Gesamte Med de U Chir* 40:592, 1928.
 5. Belt, E.: Leonardo the Anatomist. Lawrence, Kansas. The University of Kansas. p. 59, 1955.
 6. Bettex, M., Genton, N., and Schärli, A.: Uretrocystoneostomy in Vesicoureteric Reflux. *Arch Dis Child* 41:160, 1966.
 7. Bischoff, P.: Megaureter. *Brit J Urol* 29:416, 1957.
 8. Blum, H.: Physiology and Pathology of the Ureters. *Z Urol* 19:161, 1925.
 9. Brattstrom, E.: An Unusual Case of Foreign Body in the Kidney. *Acta Chir Scand* 62:56, 1927.
 10. Bumpus, H. C.: Urinary Reflux. *J Urol* 12:341, 1924.
 11. Edelbrock, H. E., and Skaint, L. B.: Sliding Roof Ureteral Meatoplasty. *J Urol* 91:496, 1964.
 12. Gruber, C. M.: Function of the Ureterovesical Valve and the Experimental Production of Hydronephrosis without Obstruction. *J Urol* 23:161, 1930.
 13. Harrison, R.: On the Possibility and Utility of Washing out the Pelvis of the Kidney and the Ureters through the bladder. *Lancet* 1:463, 1884.
 14. Hutch, J. A.: Vesicoureteral Reflux in the Paraplegic: Cause and Correction. *J Urol* 68:457, 1952.
 15. Hutch, J. A.: Theory of Maturation of the Intravesical Ureter. *J Urol* 87:534, 1961.
 16. Hutch, J. A., Ayres, R. D., and Noll, L. E.: Vesicoureteral Reflux as a Cause of Pyelonephritis. *Amer J Obstet Gyn* 87:478, 1963.
 17. Johnston, J. H.: Vesicoureteral Reflux. *Ann Roy Coll Surg Eng* 30:324, 1962.
 18. Kelly, H. A.: The Reflux of Air into the Ureters. *Amer J Obstet Gynec* 40:468, 1899.
 19. King, L. R.: Editorial Comment in the Yearbook of Urology. Chicago. Year Book Pub p. 225 1965-1966.
- 20-42 May be secured from the author or the reprints.

My First Consultation

My first medical consultation was a curious experience. In a severe case of pneumonia in an elderly lady I called in consultation a kind-hearted physician of high standing who had been present in Cincinnati at the time of my father's fatal illness. This gentleman, after seeing the patient, went with me into the parlour. There he began to walk about the room in some agitation, exclaiming, 'A most extraordinary case! Such a one never happened to me before; I really do not know what to do!' I listened in surprise and much perplexity, as it was a clear case of pneumonia and of no unusual degree of danger, until at last I discovered that his perplexity related to *me*, not to the patient, and to the propriety of consulting with a lady physician. I was both amused and relieved. I at once assured my old acquaintance that it need not be considered in the light of an ordinary consultation, if he were uneasy about it, but as a friendly talk. So, finally, he gave me his best advice; my patient rapidly got well, and happily I never afterward had any difficulty in obtaining a necessary consultation from members of the profession.*

*Elizabeth Blackwell: Pioneer Work in Opening the Medical Profession to Women, London, 1895.

Hearing Aid Referral

THE PRIMARY problem of hearing aid referrals seems to be one of a lack of information on — *what to do* — with the hard-of-hearing patients who cannot be helped by medical or surgical means. These patients are often left to the mercy of the hearing aid salesmen, with little more counselling than: "You need a hearing aid." After this meager recommendation the patient usually ends up with a high-priced hearing aid, which he often does not wear due to an inadequate fitting.

This problem of "blind" hearing-aid referrals has been reduced by the availability of professionally trained personnel in the larger Otolaryngology Practices and in University Speech and Hearing Clinics. At these facilities, specific recommendations for hearing aids are made by Audiologists who hold a Ph.D. or an M.A. Degree. Briefly, a patient receives initial counselling in regard to hearing aid wear, complete speech testing to assess the feasibility of hearing-aid wear, recommendation for a hearing aid, and a follow-up examination and counselling after the patient has been exposed to hearing-aid use.

Otologic and Audiologic Evaluation

Usually, a potential hearing-aid user has had an examination for his hearing problem prior to his purchase of a hearing aid. However, this is not always true and many hard-of-hearing patients have worn hearing aids for several years when an operation could have alleviated their problem.

Middle Ear Pathology

A good example of this is the patient with otosclerosis who has a good chance of gaining normal hearing after stapedectomy. A similar situation exists in cases with middle-ear effusion. A serous otitis media, unless treated early, can easily develop into a more complicated problem with ultimate loss of function of the complete sound-conducting mechanism (tympanic membrane and ossicular chain). From these two examples, it is obvious that a complete otologic and audiologic examination is mandatory for all potential hearing-aid wearers, especially those patients who are currently wearing hearing aids and have not had an examination.

Examination

After a complete examination has been made and all medical and surgical remedial means have been explored, the hard-of-hearing patient's problems begin. Where does he go? What kind of a hearing aid is best

Continued

for him? On which ear should he wear the aid? Should he have two hearing aids? Is his hearing loss great enough to warrant a hearing aid? All of these questions and more are common to the potential hearing-aid wearer and most of them can be handled in an initial counselling session with the patient. Specific recommendations can be made based on the audiologic examination which includes pure-tone threshold audiometry and speech testing. The pure-tone threshold examination gives a graphic representation of the patient's ability to hear sinusoidal pure tones at discrete frequencies in octaves from 125-8000 Hz. The speech testing gives important information in regard to the speech-reception threshold** and maximum speech discrimination score.**† The combined test scores give the examiner a realistic picture of how the patient can function in everyday speaking situations and also form an initial basis for the recommendation for or against hearing-aid wear.

Initial Counselling

The initial counselling session is based on the pure tone and speech testing described above. These tests give the examiner the amount and extent of hearing loss of the patient and thereby present a baseline for initial recommendation. In addition, the patient's attitude to hearing-aid use is explored in the initial counselling session, i.e.: is the patient completely negative or at least receptive to trial of a hearing aid. Questions such as those stated above are answered at this time (type of aid† — which ear — etc.) and of course differ for each hard-of-hearing patient. For example, the recommendations for different age groups (the young child versus the adult) would obviously be different, each having their own esoteric aspects.

Hearing Aid Recommendation

Following initial counselling, a hearing aid is recommended usually by one of two methods.

Method One

This method involves trying several different hearing aids on the patient, each of which is tested by speech in a soundproof room through a loud speaker. The hearing aid with the best speech score is then recommended for the patient.

Method Two

This method consists of recommending a hearing aid based on audiometric testing which is "custom-fitted" to the hearing loss. In this method the hearing aid is then worn on a trial basis for two or three days and the patient is tested in a sound field following his trial to give an objective score of his performance with and without the hearing aid. By using this method the patient has the added advantage of knowing how he

*The speech reception threshold is the sound pressure level at which the patient can repeat simple spondee words. The speech reception threshold is measured in decibels from the point at which the average normal ear speech reception threshold has been established. This point is called 0 speech reception threshold. Experimentation has established the average normal speech reception threshold to be about 18-20 decibels above the standard physical reference pressure of 0.0002 dyn/cm².

**The maximum discrimination score is measured by administering lists of so-called phonetically balanced words at levels well above the patient's speech-reception threshold. These lists contain 50 monosyllabic words, chosen scientifically in order that each list will contain samples of speech sounds in the same proportion in which they occur in everyday speech.

†Currently there are four basic types of hearing aids: (1) behind-the-ear models, (2) in-the-ear models, (3) eye-glass models, and (4) body-worn models.

would function in his everyday environment, in addition to objective measurements of his performance with and without his hearing aid. Further research will indicate which method will be generally adopted.^{1,2,3}

Follow-Up Counselling

Whatever method of recommendation is used, it is extremely important that the patient receive adequate follow-up counselling in regard to hearing-aid wear. Adjustment to the hearing aid is critical, and if the patient is not counselled in this regard, he may not wear the aid and thus not receive the benefit he should from adequate amplification. In addition, he suffers the monetary loss incurred from the purchase of an expensive prosthetic device that is not used. Counselling should also be left open-ended and not be a one-shot affair. The patient should feel free to come in and discuss any electro-mechanical problems that arise with his hearing aid or specific adjustment problems that become evident with continued use of the aid.

Summary

The problem of proper hearing aid referral is in providing information on the existence of facilities with professionally trained personnel where hearing-aid recommendations can be made. The potential hearing-aid user should receive a complete audiometric examination, initial counselling on hearing-aid use, recommendation for a specific hearing aid and follow-up testing and counselling. The benefits of such a program for the potential hearing-aid wearer, in contrast to "blind" hearing-aid referrals, are obvious.

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References

1. Carhart, R.: Hearing Aid Selection by University Clinics. *J Speech Hearing Dis.* 15:106, 1950.
2. Davis, H., Hudgins, C. V., Marquis, R. J., Nichols, R. H., Peterson, G. E., Ross, D. A., and Stevens, S. S.: The Selection of Hearing Aids. *Laryngoscope* 56:85, 1946.
3. Davis, H., Stevens, S. S., Nichols, R. H., Hudgins, C. J., Marquis, R. J., Peterson, G. E., and Ross, D. A.: *Hearing Aids, An Experimental Study of Design Objectives.* Cambridge: Harvard Univ. Press, 1947.
4. Hirsh, I. J.: *The Measurement of Hearing.* McGraw-Hill Book Co., Inc., New York, 1952.

Remedies Derived from the Lion

Lion's fat, mixed with oil of roses, protects the skin of the face from all kinds of spots, and preserves the whiteness of the complexion; it is remedial also for such parts of the body as have been frozen by snow, and for swellings in the joints. The gall, used as an ointment in combination with water, improves the eyesight, and, employed with the fat of the same animal, is a cure for epilepsy; but a slight taste only must be taken of it, and the patient must run immediately after swallowing it, in order to digest it. A lion's heart, used as food, is curative of quartan fevers, and the fat, taken with oil of roses, of quotidian fevers. — Pliny.

Business is business.

Says who?

Says too many people.

You've probably heard it yourself many times.
It's used to justify almost *anything*.

But how many times have you ever questioned this attitude or raised your voice in protest? An idea like this takes root just because not enough people do anything to stop it.

If you have ever asked yourself "Why doesn't someone do something about it?" you're talking to the right person. You.

It won't be easy. Sometimes you'll need encouragement. The kind you'll find in your place of worship.

Here you'll discover you're not alone. That, in itself, can give you the strength to say "Says who?" once in a while when it needs to be said.



Religion in American Life

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Grand Rounds

*First Stage Coagulation Disorders**

OLE JERDE, M.D.
Medical Resident

NUMEROUS ADVANCES have been made in recent years regarding the knowledge of the coagulation mechanism. Certainly the improved laboratory procedures, various assays, standardization of technique, as well as better communication between researchers here and abroad have been major reasons for these advances. As discoveries of various factors were made in countries throughout the world, different terminology was used to identify these factors. In 1959 there were at least 64 synonyms for ten distinct clotting factors.¹ Standardization of the nomenclature is a great relief to the non-coagulationist.

The purpose of this paper will be to discuss the evaluation, diagnosis, and treatment of first-stage coagulation disorders.

Mechanism of Coagulation

The Figure from Kerr¹ depicts the coagulation scheme and is similar to that found in many textbooks. The factors exist in the inactive form in the circulation and are enzymatically activated during coagulation. MacFarlane² states that the Hageman factor (XII) is activated by coming in contact with surfaces and substances other than the vascular endothelium. The activated Factor XII enzymatically activates Factor XI which, in turn, leads to activation of Factor IX. This same process continues through the first five reactions and has been termed the "enzyme cascade" by this author.² Factor X can be activated both in the intrinsic as well as in the extrinsic system by contact with tissue factor and Factor VII.¹ Information about Factor V is incomplete, but this may be a proteolytic type of activation. Phospholipid is involved in the activation of Factor V, and probably in that of Factor VIII as well.² Calcium is also needed, but the exact site of action is not known. Variations in the serum calcium level

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, October 18, 1966.

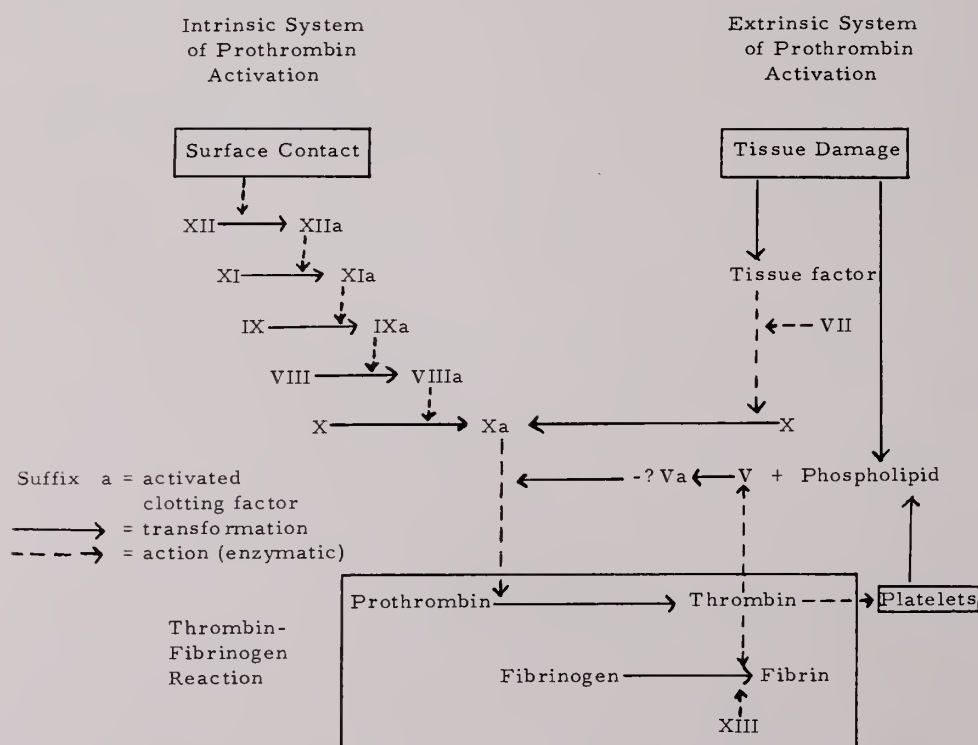
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do not alter the speed of reaction. Most of the actual time involved in coagulation occurs in the first stage.

Disorders of First Stage Coagulation

Deficiencies in the clotting factor can be divided into two groups: acquired and hereditary. As a general rule acquired coagulopathies may affect more than one factor while congenital disorders are of a single deficiency.³ However, with improvement in laboratory techniques, inherited deficiencies of more than one factor have been reported and will be discussed later. In adult medicine the most common acquired coagulopathies are due to anticoagulants and liver disease.³ Levels of Factors VII, IX, and X, in addition to prothrombin, are all decreased by the coumadin type of drugs. These have been termed the vitamin K-dependent factors,⁴ since vitamin K is essential for their synthesis in the liver. Severe liver disease can cause a deficiency of the above four factors. Factor V is produced in the liver and may be deficient in severe liver disease.³ While it is generally associated with disease states producing hypoprothrombinemia it is not dependent on vitamin K for production.

Factor XII deficiency was first discovered by Ratnoff and Colopy⁶ in 1953 in an asymptomatic man who was found to have a prolonged clotting time. He had had operations and dental extractions but had not had bleeding problems. Other reported cases revealed no or minimal clinical problems.⁷ A few cases have been reported in which ecchymoses and severe hemorrhage did occur.³



*Kerr, C. B., *Journal of Medical Genetics*, 2:256, 1965.

Figure

In the early 1950s it was found that hemophilia was not a single disease but rather three different disease entities which presented with very similar clinical pictures.^{8,9} These factors are easily separated by the use of serum and barium sulfate-treated plasma. Factor VIII deficiency (AHG) is corrected by barium sulfate-treated plasma but not by serum; Factor IX deficiency (PTC) is corrected by serum but not by barium sulfate-treated plasma, while Factor XI deficiency (PTA) is corrected by both.⁸

Factor VIII and IX deficiencies are sex-linked recessive inherited disorders while PTA deficiency is of autosomal inheritance.¹ Kerr¹ states that PTA deficiency is an incomplete recessive defect while Conrad et al.¹⁰ believe it to be a dominant autosomal disorder, affecting both sexes.

It was thought that while females were carriers and would pass the trait on to their offspring they themselves were not clinically affected. The belief was that this was a lethal condition for the fetus.¹¹ In recent years, however, several cases of homozygous hemophilia in females have been reported.¹¹ These authors reviewed the literature and presented a woman who had had bleeding difficulties since childhood. Judging from family analysis this patient was thought to be a heterozygote. Factor VIII levels were determined and found to be very low. This is a very rare occurrence, and it was postulated that a mutant gene may have been responsible.

Conrad et al.¹⁰ reviewed the literature regarding the relative incidence of these three deficiencies and found that AHG deficiency accounted for 64 to 86 percent, PTC deficiencies range from 11 to 18 percent, and PTA deficiencies, 1 to 18 percent of the total. Conrad reported 82 cases in his series and found that AHG deficiency accounted for 16 percent, PTC deficiency for 4 percent, and PTA deficiency for 80 percent. His series probably does not reflect a true cross section of the population since he investigated military personnel as well as their dependents, and states that people with overt AHG and PTC deficiencies were rarely seen. These authors feel that of these three disorders, PTA deficiency is more often benign and easily missed unless complete diagnostic studies are made. Of their 65 patients with PTA deficiency, 22 cases were asymptomatic, but were evaluated because of a family history of bleeding disorders. Most of the other patients had histories suggestive of a clotting defect, or presented with bleeding problems. The mild forms of these three disorders have been termed the "occult hemophilias."¹² These are patients who have few symptoms, but who may bleed following trauma or surgery; and many cases have been discovered at the operating table. Patients with Factor VIII and IX deficiencies have been separated into three groups depending on the severity of the clinical picture, as well as factor levels.¹ Severe hemophilia includes those with factor levels of 0 to 1 percent. The coagulation time is markedly prolonged and the patient will have had severe bleeding since early childhood. Spontaneous hemorrhages are common with hemarthrosis, hematomas, and hematuria, most of which will demonstrate permanent disabilities and should present no problems in diagnosis. In moderate hemophilia the factor levels range from 1 to 3 percent and the clotting time is only slightly prolonged. Bleeding does occur but is generally less frequent and less severe with fewer disabilities. In the third group are the mild or occult hemophiliacs with factor levels of

Continued

3 to 30 percent and a normal clotting time. These patients rarely have spontaneous hemorrhages and often live a normal life. The mechanism which controls the production of these factors is unknown,¹² but multiple alleles may be involved. This might explain the broad range of factor levels found in normal people as well as in bleeders.

Factor X deficiency (Stuart's disease) is a very rare bleeding disorder with only 20 proven cases reported in the literature.¹³ Clinically this disease is very similar to the previously described disorders with spontaneous hemorrhage and bleeding following trauma. Hemarthrosis occurs, and in the case presented the patient required transfusions for excess menstrual flow.¹³ Clotting time, prothrombin time, and the partial thromboplastin tests were abnormal. Specific assays revealed less than 1 percent concentrate of Factor X. This is an autosomal recessive inherited defect.^{1,13} The heterozygotes, while clinically normal, were easily distinguished on the basis of Factor X level.

Adequate Factor VII levels are required for normal hemostasis and it is thought that this factor functions only in the extrinsic system in the presence of tissue juice.¹⁴ While there is some disagreement about inheritance, most studies would indicate that this is an autosomal recessive trait, with equal sex predilection.^{1,15} While the carriers have decreased factor levels to 50 percent of normal, they do not have a bleeding tendency.¹⁵ Deficiencies of this factor cause clinical bleeding problems which are very similar to other first stage defects.¹⁵ While bleeding after dental extractions is quite severe, several patients have had major surgery without blood loss.^{16,17} Even though blood levels are low, there is a wide variation in the severity of clinical bleeding problems,¹⁷ and the mechanism here is not known. Of interest is that one of Hall's¹⁷ patients died from pulmonary emboli illustrating that this isolated defect does not protect against venous thrombosis. Vitamin K preparations, even in massive doses, are of no help in the congenital condition.¹⁶

Congenital Factor V deficiency (labile factor), while rather rare, has been reported from various areas in the world.¹⁸ This is an autosomal gene, probably recessive, with equal sex incidence.¹ The heterozygote, while having slightly prolonged prothrombin time, is not clinically affected. Clinically the bleeding is generally the capillary type with epistaxis, purpura, and easy bruising. Trauma, surgery, and dental extractions may be followed by severe hemorrhage; however, O'Brien¹⁹ reported a patient who had had several operations without bleeding, but had had hemorrhage after dental extractions. Specific assays showed very low levels of Factor V. Vitamin K does not alter the prothrombin time and has no beneficial effect clinically.

While very rare, patients having multiple deficiencies have been reported.^{20,21} Statistically, the incidence of a combined deficiency of both Factor VIII and IX would be one in ten million.²¹ These authors studied a family in which several members had PTA deficiency, AHG deficiency, or increased vascular fragility. One of the family members was thought to have all three deficiencies. Verstraete et al.²⁰ studied four different families with PTC deficiencies and found a decrease in Factor VII activity in all patients with the disease. It is thought that proconvertin (VII) is bound to an inhibitor while in the inactive form, and that activation occurs by removal of this inhibitor. From laboratory studies it appears

that Factor IX may have a role in the activation of Factor VII. These authors feel that in patients with PTC deficiencies there may be delayed activation of Factor VII rather than an actual deficiency. Inhibitors and circulating anticoagulants may be present and complicate the picture even more.²¹

Diagnosis of First Stage Defects

History

As with most medical problems a detailed, carefully taken history is the most important part of the evaluation,²² but, as noted previously, there are mild forms of these diseases in which there may be no history of bleeding tendencies. Another point is that the patient with mild bleeding tendencies may have learned to live with his disease and does not regard himself as a bleeder. A great deal of medical judgment is needed to evaluate whether a bruise is significant or what frequency of epistaxis is abnormal. Also the reliability of the patient must be considered, and at times a history may be misleading.²³ Specific questions must be asked regarding the frequency of epistaxis and the degree of bruisability.²² Questions must be asked about circumcision, dental extraction and other operations, hematomas following injections, trauma, hemorrhage from the genitourinary and gastrointestinal tract as well as hemarthrosis.²² Questioning must also include menstrual history. A detailed family history should be taken including an inheritance pattern, since over 90 percent of congenital bleeding disorders are either Factor VIII or IX deficiencies²² and are sex-linked. A negative family history, however, does not rule out bleeding problems, since 25 percent²² to 50 percent²³ of hemophiliacs will give a negative family history. A thorough physical examination with particular emphasis on the skin and joints must be done on all patients.

If the history is at all suggestive of a bleeding disorder a complete laboratory evaluation must be done.

Laboratory Studies

The whole blood coagulation time has been discontinued as a screening test for bleeders by several authors^{10,24,25} since it is often normal in mild forms. Diamond and Porter²⁵ reported on 19 patients with normal bleeding and clotting times; however, special tests proved that all 19 patients had either PTC or AHG deficiencies. They also reported nine cases with abnormal Lee-White tests, in which other special studies were normal. Since the test was of no help and often misleading, it should be discontinued for screening patients.²⁵

The partial thromboplastin time (PTT) test was originally described by Langdell, Wagner, and Brinkhouse in 1953,²⁶ and has proved to be a good screening test, which can be used to detect deficiencies of Factors XII, XI, X, IX, VIII, and V in addition to fibrinogen and prothrombin.²⁷ The PTT test is not sensitive to Factor VII deficiencies, but this can be evaluated by the one-stage prothrombin time. The PTT test will also be abnormal if an inhibitor is present.²⁷

The prothrombin time (one-stage) is sensitive to deficiencies of prothrombin Factor VII, V, X and fibrinogen²⁴ and is recommended for all possible bleeding problems.

Continued

The PTT test does not detect platelet abnormalities so that platelet count, bleeding time, tourniquet test, and clot retraction may be needed for complete evaluation.²⁴

Conrad et al.,¹⁰ in evaluating PTA deficiencies, found that the thromboplastin generation test was more accurate than the PTT or prothrombin consumption test, and recommended that the TGT be done on all possible bleeders.

The coagulation work-up as proposed by Krivit and White²⁴ using the PTT test, prothrombin time and platelet functions should detect most clinical problems. If these tests are borderline and the history suggestive of a bleeding disorder, further tests can be done.

Treatment

In the past, fresh blood, fresh plasma or fresh-frozen plasma has been used for the control of acute bleeding episodes in Factor VIII-deficient patients. Fresh plasma will generally control the bleeding in soft tissue injuries; however, it is difficult to maintain adequate Factor VIII levels to prevent hemorrhage during surgery or after dental extractions by the use of plasma alone.²⁸ It may take one liter of fresh plasma to raise the AHG concentrates to 15 percent in the severe hemophiliac,²⁹ and concentrations of 25 to 40 percent are required during surgery and following dental extractions to achieve adequate hemostasis.^{28,29} Since the life of AHG in the circulation is rather short, frequent infusions are necessary and may lead to congestive heart failure. The development of concentrates of AHG have made surgery a safer procedure for the hemophiliac.

McMillan et al.³⁰ report their experience with the use of the Fraction I of Cohn, which is a Factor VIII concentrate containing significant amounts of fibrinogen. Factor VIII is seven times as concentrated as in normal plasma, which considerably decreases the volume load. Their results were quite good except where therapy was stopped too soon. Oozing occurred but promptly ceased when more of the concentrate was given. Levels of fibrinogen up to 1,000 mg./100 ml. plasma were observed and two patients developed hemolysis, which stopped when the fibrinogen returned to normal levels. One case of hepatitis occurred, but this patient had also received blood and plasma.

In Britain both bovine and porcine concentrates are readily available and frequently used where large amounts are needed.³¹ Good control was obtained in their series; however, these are antigenic and can be given for only a limited period of time.

Pool and Shannon³² report on a method of producing a cryoprecipitated* AHG concentrate which can be done in the local blood bank. This is highly concentrated with 30 times the level of AHG compared to frozen plasma. High blood levels were easily maintained in the one case studied by giving the concentrate every 12 hours. No adverse reactions were noted.

Webster et al.³³ report on the use of a glycine precipitated concentrate. There is from three to eight times more AHG per gram of fibrinogen compared with the Cohn fraction. Large amounts were infused without any side effects. Following the initial infusion it had a half-life of eight hours, but after repeated infusions the half-life was 14 to 16 hours. Theoretically the difference is due to diffusion into the extracellular compartment.

Because of individual variation no simple dosage schedule can be de-

*See Test Your Word Score Page 687.

terminated.²⁸ Bleeding and infection will increase the amount needed. For the surgical patient Tornay suggests giving therapy every eight to 12 hours for 12 to 16 days following the operation. While specific assays for Factor VIII levels are the best guide for controlling the patient,²⁸ the PTT test is of help.³⁴

There are no concentrates available for treating PTC deficiencies; therefore fresh plasma or blood must be used.²⁹ Stored plasma may be used; however, fresh is preferred. The half-life of Factor IX ranges from 18 to 30 hours with an average of 24 hours.³¹ Barrett²⁹ recommends giving one unit of fresh plasma every six hours following a surgical procedure until healing has occurred.

The initial half-life of Factor XI is 60 to 80 hours, and after repeated infusion a delayed second half-life is observed of up to 190 hours.³⁵ Adequate hemostasis can be achieved with either stored or fresh plasma; however, fresh plasma gives longer results.⁵

Factor X has an infused half-life of about 48 hours.³¹ The active bleeder can be controlled by plasma or serum.⁵

Factor VII, while stable in vitro, is rather short-lived in the circulation with a half-life of five hours.¹⁶ In spite of this short half-life, plasma will stop the bleeding and prevent further hemorrhage for three to four days.¹⁵ One of Mauder's patients received 19 ml. plasma/kg., then had extensive dental work without bleeding and required no further therapy.

Factor V has a survival time of 24 to 48 hours.⁵ Bleeding problems can be controlled with fresh blood, fresh plasma, or fresh-frozen plasma.^{5,18}

Case Report

A 16-year-old white male was admitted to Hennepin County General Hospital on 8/28/66 because of a swollen, painful right knee. He had twisted this knee two days before and had had progressive symptoms.

Previous Admissions

1955 — Patient was admitted because of severe, persistent hemorrhage following tonsillectomy. The Lee-White was over one hour. Prothrombin time, clot retraction and tourniquet test were normal. He was treated with fresh-frozen plasma with good response. A diagnosis of PTC deficiency was made at the University of Minnesota.

1960 — Patient was admitted because of hemorrhage following a dental extraction. Bleeding stopped after one unit of blood.

1960 — Hemarthrosis, right knee.

1961 — Hemarthrosis, right knee.

1962 — Hemarthrosis, left knee.

1963 — Hemarthrosis, left elbow.

Family History:

An uncle and one nephew have bleeding tendencies. One nephew died at age three following skull fracture.

Physical Examination:

The physical examination was normal except for the swollen tender right knee. There was no warmth or redness present.

Laboratory Data:

PTT on 8/28/66 was 59. Control 46 Prothrombin time 15.2. Control 12.6.

Hospital Course:

The patient was treated with ice packs, rest and elevation. He received two units of fresh-frozen plasma on the day of admission and two units the following day. Convalescence was slow; however, the right knee was markedly improved and was without pain or swelling on discharge.

Venereal Disease A Serious National Problem, Says AMA

Venereal disease is spreading so rapidly that it now represents this nation's most urgent communicable disease problem.

VD is hitting particularly hard among teenagers and young adults, according to the American Medical Association.

The venereal diseases are infecting about two Americans a minute—3,000 a day, or 1,100,000 a year. Cases of infectious syphilis have almost tripled in this country in the past five years. More than a million

new cases of gonorrhea are developing annually.

VD can blind, cripple, and even kill.

The ravages of venereal diseases are all needless tragedy, says the AMA, because both syphilis and gonorrhea can be avoided. If contracted, they can be cured by prompt medical treatment.

The cure for both diseases—penicillin—has been available since 1943. Any family physician or public health clinic can administer

prompt treatment.

Venereal disease is caused by intimate personal contact.

Complacency, ignorance, and a free-and-easy attitude toward moral standards are partly responsible for the spread of VD; the increasing use of alcohol, especially among young people, also plays a role.

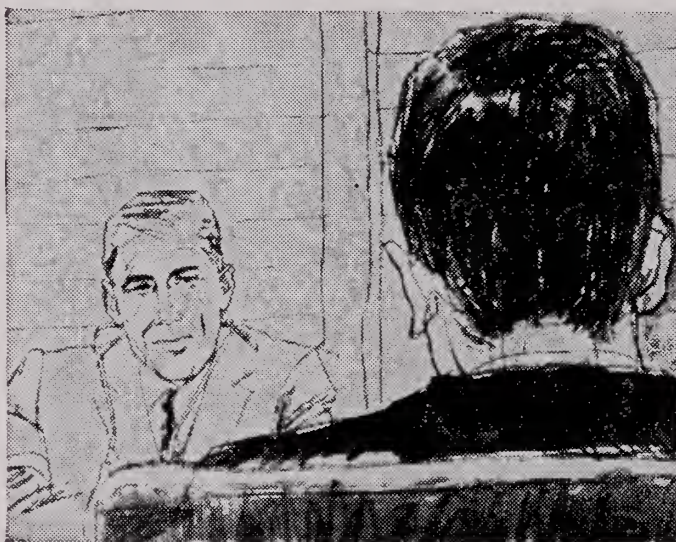
Authorities believe, however, that thousands of young people simply aren't aware of the dangers of VD. Once infected, they are complacent about treatment.

One of the first signs of syphilis may be a painless, ulcerating sore. Gonorrhea produces inflammation of the genital and urinary tracts, and a discharge of pus.

A person may contract syphilis and be unaware that he has the disease. After the first symptoms, the germs may remain hidden in the body for as long as 20 years before any damage is discovered. Then the person may become crippled, develop heart disease, blood vessel disease, blindness, or show mental symptoms. Even death may result from this hidden stage of syphilis.

If left untreated, gonorrhea may be responsible for arthritis, endocarditis, sterility, and blindness.

If a person suspects he may have contracted venereal disease, he should go to a physician immediately.



VD should be treated promptly by a physician.



Abstracts, Briefs and Commentaries

THALIDOMIDE AND CONGENITAL CLEFT DEFORMITIES

Among the suspected nongenetic factors in the etiology of cleft lip and palate in humans, the intake of various drugs in early pregnancy deserves attention. Aminopterin has been used to induce abortions. When abortion failed to occur, multiple congenital malformations in the child have occurred, among them cleft lip and palate. The typical embryopathy described in West Germany, Denmark, and other countries revealed multiple severe malformations. Nine women in Copenhagen requested abortion because they had used Thalidomide. Six had their pregnancy aborted. Three, because their requests were too late, completed pregnancy. One child was normal, one had bilateral aplasia, and the third had a cleft lip and palate. Since this publication three or four more similar deformities have been reported in Sweden and three or four in Japan.

The authors state that there has been a definite increase of cleft lip and palate. In Denmark this has been reported statistically (Frogh-Andersen 1963) : at present one in 500 newborn.

They suggest the possibility of such deformities resulting from other drugs during the early months of pregnancy. "This is not less probable when we consider the enormous abuse of tablets of nearly all kinds which has taken place during the last few decades, in most civilized countries: particularly sedatives, hypnotics, tranquilizers, and appetite-depressing drugs." Although Thalidomide is not available, a multiplicity of new drugs are on the market.

Stanley R. Maxeiner, M.D.
Minneapolis, Minnesota

P. Fogh-Andersen: Thalidomide and Congenital Cleft Deformities. *Acta Chir Scand* March, 1966.

UMBILICAL VEIN ANGIOGRAPHY

A fascinating study of 60 cases of transumbilical catheterization of the portal vein are presented. Operative technique includes a small incision in the umbilicus through the linea alba. The umbilical vein remnant is found extraperitoneally. Amazingly, the lumen is merely collapsed but not adherent. A catheter is then advanced into the portal vein.

Continued

ABSTRACTS, BRIEFS AND COMMENTARIES

Pressure measurements can be made, and injection of radiopaque contrast material can outline the portal vein, the splenic vein and collaterals. There has been essentially no morbidity in 60 consecutive such catheterizations. This technique would be of particular benefit in cases where the spleen is not available for percutaneous puncture and study.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Kessler, Richard E. and Zimmon, David S.: *Radiology*. 86:5:841, 1966.

ECHINOCOCCOSIS OF THE LIVER AND LUNGS ANALYSIS OF NINETEEN CASES

These authors present 19 cases of echinococcosis cyst of the liver and lungs. The remarkable facet of this report is that 18 of the cases were contracted within the state of Utah. The life cycle of the echinococcosis is reviewed. The treatment recommended was complete excision of the cyst, whether in liver or lung, whenever possible. Marsupialization of the cyst is also recommended in cases where excision is impossible. A review of chemical sterilization of the interior of the cysts concludes that hydrogen peroxide and iodine are the most effective drugs. The increasing incidence of hydatidosis should be of great concern to both physicians and public health officials.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

Hicken, N. Frederick, McAllister, A. James, Carlquist, John H., Madsen, Frank. *Amer J Surg* 112:6:823, 1966.

OSTEOPOROSIS

The decrease in bone mass observed in osteoporosis results from an imbalance between bone formation and bone resorption and may arise from (1) reduction in bone formation while bone resorption remains unchanged, (2) normal bone formation associated with increased bone resorption, (3) decrease in bone formation in addition to increased bone resorption, (4) an increase in bone formation with a greater increase in bone resorption, and (5) a reduction in bone formation greater than a decrease in bone resorption. Recent studies suggested that bone formation is normal or slightly increased in postmenopausal or senile osteoporosis, and that, instead, bone resorption is increased. Dietary studies in England and the United States indicate that patients with osteoporosis ingest less calcium in their diets than do their nonosteoporotic contemporaries. The osteoporosis seen in hypercortisonism seems due mainly to a decrease in bone formation. In the osteoporosis accompanying hyperthyroidism, increased bone resorption is the important factor in pathogenesis. On the other hand, in such conditions as osteoporosis of disuse, the decrease of bone mass is due primarily to a reduction in new bone formation. Relief of pain and improved retention of calcium have been demonstrated after therapy with anabolic hormones.

Bassan, J., Frame, B., and Frost, H.: *Ann Intern Med*: 58:539, 1963.



Book Reviews

If the truth be not diffused, error will be; if God and his word are not known and received, the devil and his works will gain the ascendancy; if the evangelical volume does not reach every hamlet, the pages of a corrupt and licentious literature will; if the power of the gospel is not felt through the length and breadth of the land, anarchy and misrule, degradation and misery, corruption and darkness, will reign without mitigation or end. — Daniel Webster

APPRAISAL OF CURRENT CONCEPTS IN ANESTHESIOLOGY, Vol. 3 — 1966. Edited by John Adriani, M. D. C. V. Mosby Co., St. Louis, Mo.

This third volume in the series bearing the same title again results from the program initiated at Charity Hospital in New Orleans in the teaching of anesthesiology. Trainees, and occasionally staff personnel, prepare papers on subjects of importance to those concentrating in this field, and these papers are then reproduced for distribution to all the department members. Dr. Adriani has edited a number of these reviews which are of the greatest interest and/or importance, and has compiled them in this book, thereby making this valuable information available to many others than just his staff.

The papers in this newest volume cover a variety of topics, such as pulmonary function tests, irreversible shock, use of pacemakers and cardiac monitoring equipment, drugs in cardio-respiratory resuscitation, and a worthy three-part review on the absorption, distribution, and elimination of volatile anesthetic agents. The book concludes with monographs for teachers in the field, suggesting how to instruct trainees and what they should know, and for the trainees it gives helpful pointers on how to prepare for and take written examinations. The basic concept of these papers is to review the early thinking and fundamental facts on a subject and then to expand this knowledge with a succinct review of the recent literature on that subject. Thus, all the papers represent the midpoint in thinking and knowledge in their area, for they are more current than the latest texts in the field and only slightly less current than the newest literature.

This latest edition of **CURRENT CONCEPTS** is better than its predecessors, for it includes topics of greater and, in many instances, more practical interest to the practitioner, and the approach in writing tends to favor the clinical more than the academic. The

book could be of interest to many others besides just those practising or teaching anesthesiology.

Richard O. Burmeister, M.D.
Midway Hospital
St. Paul, Minn.

PRIMER OF PERIPHERAL VASCULAR DISEASE — Travis Winsor, M.D. and Chester Hyman, Ph.D. Lea & Febiger, Philadelphia, 1965.

This monograph on peripheral vascular disease is well organized and adequately documented.

The chapter dealing with methods of study includes a number of items which deserve particular attention for the physician who is interested in making a thorough study of peripheral vascular abnormalities.

A bibliography is attached at the end of each chapter and the indexing is adequate.

The book is well bound.

Carl O. Rice, M.D.
Minneapolis, Minnesota

QUESTIONS AND ANSWERS IN ORTHOPAEDICS — Goodman and Schoedinger, III, Publication Date 8/66, Price \$9.85, C. V. Mosby.

This "book" consists of 213 pages of multiple choice, single answer, multiple choice-multiple answer, and true-false questions on orthopaedics. The questions provide an excellent detailed general review of the field. The answers are in the back of the book and references with page numbers are given for each question.

The authors are currently residents at Barnes Hospital-Washington University. The book is written specifically for students, interns, residents, and board aspirants. Much effort has gone into compiling and formulating these questions and this fine effort should be rewarded by a wide circulation.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

Should You Lease Equipment?

As is the case with many questions of an economic nature, there is no standard "yes" or "no" answer to this question of leasing versus owning equipment. Each such question must be analyzed in terms of the specific terms and conditions.

Leasing of equipment has developed over the past few years primarily out of a need for working capital by business and industry requiring abnormally large financial outlays for plant and equipment. Frequently these concerns can use their limited capital to better advantage in phases of their business other than committing it semi-permanently to equipment.

In general, however, leasing companies are organized for profit. Certain volume purchase economies may be realized by the leasing companies, but in the final analysis, the lease payments must not only cover the cost of the equipment, but also financing and administrative costs — and a reasonable to excessive profit to the leasing company.

Many leasing companies use "tax savings" as a sales incentive. This is more imaginary than real, since the entire cost of purchased equipment may be recovered through regular or accelerated depreciation, just the same as the entire rental payment may be deducted. Usually, greater deductions through leasing result from the simple fact that the cost is greater.

For the individual interested (often ill-advisedly) in maximum possible tax deductions, such things as accelerated depreciation, 20% first-year depreciation and the 7% investment credit make it possible to recover as much as 75% of the cost of an asset in the first five years of its ownership. Frequently in the case of new practices, new partnerships or generally rising income, it will be advantageous to spread the deductions for recovery of cost on an asset over the longest possible period — a situation which does not lend itself to leasing.

In evaluating the specific merits of a leasing proposal, there are two primary considerations which must be scrutinized very carefully. First, what is the total cost of the asset to me if I lease and if I buy the asset? Second, what is the tax status of the payments I make?

A lease agreement which we evaluated recently clearly illustrates both of these factors. The lease was for five years and provided for rental payment of \$110 monthly. At the end of the five-year period, the Doctor could exercise an option to purchase the X-ray machine for \$300. An outright purchase of the machine would cost \$5,000.

Over the five-year lease period, this Doctor would pay \$6,600 in rental payments and then a final option payment of \$300 — a total of \$6,900. A cash purchase would require \$5,000, or \$1,900 lease. Even assuming a five-year credit purchase at 6%, the total principal and interest payment would be \$96.67 per month or a total of \$5,800. In other words, the Doctor is paying a premium of \$1,900 to lease if he has adequate funds available — or a premium of \$1,100 if he has to finance 100% of the purchase over five years.

Reduced to monthly terms, it would be over \$13 per month cheaper to buy than to lease.

Evaluation of the tax status of this particular contract is even more disappointing. The Internal Revenue Service screens these leases very carefully and requires that they have more aspects of a lease than a purchase agreement. A very important factor in this screening is the option price. If it is representative of fair market value at the option date, the arrangement will probably stand up as a lease. However, investigation of this particular contract disclosed that the value of a five-year old X-ray machine of this type could be estimated at \$2,400 to \$3,000. Comparison of this value with the \$300 option price indicates clearly that the option price is nominal.

In this case, after agreeing to pay an unreasonable rental price, the Doctor was faced with the probability of the Revenue Service classifying the transaction as a "Conditional Sales Contract" and therefore, requiring that the cost be amortized through depreciation over a ten-year life.

From a depreciation standpoint, the Doctor could take the 20% first-year depreciation of \$1,000 plus \$800 ten-year accelerated depreciation. In the second, third, fourth and fifth years, he could take an additional \$1,890 depreciation for a total of \$3,690. He could also take the \$800 interest paid over the five-year period.

Finally, he would be entitled to \$350 Investment Tax Credit — equal to a \$700 deduction in his 50% tax bracket. His total deductions would be equivalent to \$5,190 of the \$5,800 cash outlay over the first five years or 89½%.

On the lease he would pay out \$6,900 which would entitle him to \$5,090 depreciation. The \$483 Investment Tax Credit would be equal to a \$966 depreciation deduction increasing total deductions for the five-year period to \$6,056, or 87½% of the total outlay.

Obviously, this Doctor was not anxious to pay a premium of \$1,100 for a machine and then be able to deduct 2% less of that cost over the first five years.

While this is not a standard lease, it is quite typical of equipment leases from an economic standpoint. It can be generally stated that it takes a special set of financial circumstances to justify leasing instead of purchasing equipment for a Dental or Medical practice.

Only through careful evaluation of your specific circumstances and examination of the proposed lease can a determination of the validity of a leasing proposal be made. Obviously, the time for this evaluation is prior to the execution of the lease agreement.

The question of auto leasing has been dealt with in previous articles. In general, it has been concluded that unless you drive at least 25,000 miles per year — or are willing to pay a premium for the prestige of a new car each year and freedom from "ownership worries" — ownership of autos is also less costly than leasing.

William D. Huntington*
Minneapolis, Minnesota

*Northern Division Manager, Professional Management Midwest.

Derivatively Speaking

Trochlea — from Greek *trochilia* (pulley)

114th Annual Meeting

Annual Meeting Program Set

A wide range of events including scientific sessions, round table luncheons, technical and scientific exhibits, banquets, a golf tournament, and business sessions await physicians attending the 114th Annual Meeting of the Minnesota State Medical Association May 15, 16 and 17 in Duluth.

All of the business and scientific sessions and the exhibits will be housed in the new \$6.1 million Duluth Civic Auditorium. The House of Delegates will convene Sunday, May 14, at 2:00 P.M. in the Auditorium, and on Tuesday, May 16, at 9:00 A.M.

The new members, county officers and delegates dinner is scheduled for Sunday evening at 6:00 P.M. in Hotel Duluth. Reference committees for the House of Delegates will meet Sunday at 8:00 P.M. Committee breakfasts will be held Monday, Tuesday and Wednesday mornings at 7:30 A.M.

Golfers will meet at 10:00 A.M. Sunday, May 14, at the Northland Country Club for the annual tournament. Bridge fans will want to attend the tournament scheduled for Monday night at 8:00 P.M. at the Duluth Hotel.

The Wednesday program will be devoted to discussion of current socio-economic topics of interest to all physicians.

All physicians are respectfully urged by the Committee on Scientific Assembly to visit the scientific and technical exhibits, and to express their appreciation to the technical exhibitors who have helped to make the meeting possible.

Dialysis or Transplantation — Yes or No

Is lifesaving renal therapy too costly? Is it fair to offer the patient doomed to die from renal failure the choice of dialysis or transplantation, knowing that neither choice is available to the average patient in need

of such treatment? What are the ethical, legal and philosophical aspects involved in sustaining the life of a doomed patient by use of dialysis or transplantation?

A panel representing the legal, medical and religious aspects of this problem will present their respective views at the Medicine and Religion Scientific Session scheduled for Monday, May 15, at 2:00 P.M. Members of the panel titled "M.D., L.L.B. and D.D. — Whither Goest Thou?" are the Rev. Dr. Paul B. McCleave, Department of Medicine and Religion, American Medical Association; Thomas E. Starzl, M.D., Associate Professor of Surgery, University of Colorado Medical School, and Mr. Burr B. Markham, member of the firm of Meagher, Geer, Markham and Anderson, Attorneys at Law, Minneapolis. Eugene Scott, M.D., Chairman of the Committee on Medicine and Religion, St. Paul, will moderate the panel.

Fertility and Sterility

Alan F. Guttmacher, M.D., New York, President, Planned Parenthood Federation of America, Inc., will discuss methods of birth control at the Scientific Session, Tuesday, May 16, at 4:00 P.M. devoted to the topic "Fertility and Sterility." Doctor Guttmacher is now considered by a number of observers as having inherited Margaret Sanger's role as prime mover of birth control. Discussing "Induction of Ovulation in the Treatment of Infertility" at the same session will be William N. Spellacy, M.D., Minneapolis, Assistant Professor, Department of Obstetrics and Gynecology, University of Minnesota Medical School.

Convulsive Disorders

Two Minnesota physicians will discuss "Convulsive Disorders" at the 2:00 P.M.

Continued

session on Tuesday afternoon. The participants are A. B. Baker, M.D., Minneapolis, Director, Department of Neurology, University of Minnesota Medical School, Minneapolis, and William R. Heilig, M.D., St. Paul, specialist in Neuro-Pediatrics.

Erythroblastosis Fetalis

The 10:30 A.M. session on Tuesday will be devoted to the subject of "Erythroblastosis Fetalis" and will climax a six-week home study course in which approximately 100 Minnesota physicians were enrolled. Participants in the Erythroblastosis session are John M. Bowman, M.D., Assistant Professor of Pediatrics, University of Manitoba, and Rhinehart F. Friesen, M.D., a lecturer in Obstetrics and Gynecology at the University of Manitoba, and also a lecturer in these same subjects at the School of Rehabilitation. Attendance at this session is not limited to registrants for the course.

Cardiac Emergencies

Medical emergencies under the title "Doctor Blue — Where Are You?" will be discussed at the opening Scientific Session on Monday, May 15, at 9:00 A.M. The following physicians will discuss various aspects of cardiac emergencies: Harold Katkov, M.D., Wayzata; Carlos E. Harrison, Jr., M.D., Rochester; and Stephen M. Ayres, New York.

Iatrogenic Medical Problems — Dangerous Drugs

The 9:00 A.M. session Tuesday has the title "Iatrogenic Medical Problems — Dangerous Drugs." Participants include Raymond N. Bieter, M.D., Professor of Pharmacology, University of Minnesota, and Edward A. Carr, Jr., M.D., Department of Pharmacology, University of Michigan Medical School.

Here's How To Do It

Minnesota physicians will participate in a series of eleven five-minute "How To Do It" talks on Monday at 3:30 P.M. Physicians and their topics are as follows:—

Warts Cooking?

E. T. Ceder, M.D., Minneapolis

Constipation — Can't or Won't

Felix A. McParland, Jr., M.D., Minneapolis

The Plugged Catheter

B. J. McGroarty, M.D. St. Paul

Bloody Nose

O. E. Hallberg, M.D., Rochester

Threatened Abortion

Carl E. Johnson, M.D., Rochester

Painful Feet

Kenath H. Sponsel, M.D., Minneapolis

Contact Lenses

Theodore R. Fritsche, M.D., New Ulm

The Buzzing Ear

Barclay M. Cram, M.D., St. Paul

The Discharging Nipple

David P. Anderson, Jr., M.D., Austin

How to Inject a Painful Shoulder

Charles G. Sheppard, M.D., St. Peter

The Varicose Ulcer

Eric P. Lofgren, M.D., Rochester

Round Table Luncheons

Round Table Luncheons and physician participants scheduled for Monday at 12:15 P.M. include the following:—

The Hearing Aid Problem

Joseph H. Leek, M.D., Duluth — Leader; Craig Linnell, Ph.D., Audiologist, St. Paul.

Dialysis in the Community Hospital and the Home

J. C. Hunt, M.D., Rochester — Leader; Donald A. Duncan, M.D., Minneapolis; Fred L. Shapiro, M.D., Minneapolis; W. J. Johnson, M.D., Rochester, and Mr. Harris W. Feldick, Osage, Iowa.

Cancer Chemotherapy

B. J. Kennedy, M.D., Minneapolis — Leader; Harry F. Bisel, M.D., Rochester; and John H. Brown, M.D., Minneapolis.

Ongoing Coronary Disease

Carlos E. Harrison, Jr., M.D., Rochester — Leader; Stephen M. Ayres, M.D., New York; Wilbert J. Henke, M.D., St. Paul, and Harold Katkov, M.D., Minneapolis.

DULUTH

Field Diagnosis in Athletic Injuries

Edward D. Henderson, M.D., Rochester — Leader; E. D. Nelson, M.D., Minneapolis, and W. E. Proffitt, M.D., Minneapolis.

Annual Physical — Why?

A. Cabot Wohlrabe, M.D., Minneapolis — Leader; Karl W. Anderson, M.D., Minneapolis

The Neuter Sex

Valentine O'Malley, M.D., St. Paul — Leader, and others.

Round Table Luncheons and physician participants scheduled for Tuesday at 12:15 P.M. include the following: —

Medical and Surgical Treatment of Persistent Peptic Ulcers

Owen H. Wangenstein, M.D., Minneapolis, and James C. Cain, M.D., Rochester.

Drug Incompatibilities

Raymond N. Bieter, M.D., Minneapolis — Leader; Edward A. Carr, Jr., M.D., Ann Arbor, Michigan.

Erythroblastosis Fetalis

Peter Bartzen, M.D., Duluth — Moderator; Donald Larson, M.D., Duluth; Arthur Aufderheide, M.D., Duluth; Glen E. Holt, M.D., Duluth; John M. Bowman, M.D., Winnipeg, and R. F. Friesen, M.D., Winnipeg.

Diagnosis of the Unconscious Patient

A. B. Baker, M.D., Minneapolis.

The Thrombosed Hemorrhoid

William C. Bernstein, M.D., St. Paul — Leader; R. J. Spencer, M.D., Rochester, and John V. Thomas, M.D., Duluth.

Multiple Pregnancy

Alan F. Guttmacher, M.D., New York.



Duluth — May 15, 16, and 17

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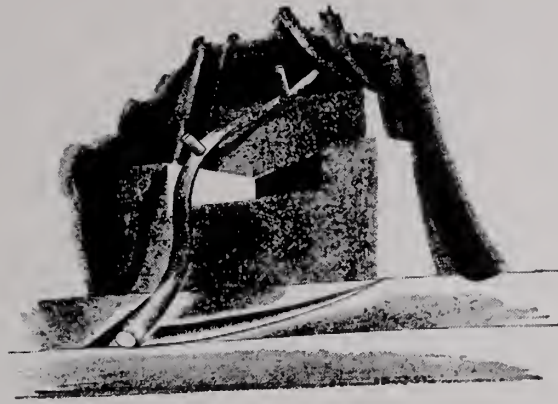
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In Memoriam

Death has nothing terrible which life has not made so. A faithful Christian life in this world is the best preparation for the next. — Tyron Edwards

ROBERT L. BOWEN, M.D.

Dr. Robert L. Bowen, 79, prominent Hibbing physician and surgeon and active civic leader, died February 26. He was the founder of Hibbing's Mesaba Clinic and participated in the organization of the former Rood Hospital in Hibbing. Born in Oshkosh, Wisconsin, Dr. Bowen had practiced in Hibbing since 1919. He was graduated from the University of Wisconsin and completed his medical education at Rush Medical College in Chicago.

He was a former member of the Hibbing Board of Education, a fellow of the American College of Surgeons, a member of the American Medical Association and Range Medical Society, and a 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by his wife and a son, Dr. Robert L. Bowen, Jr. of Eugene, Oregon.

KATHERINE A. NYE, M.D.

Dr. Katherine A. Nye, 80, life-time St. Paul family physician, died March 2. Born in Zumbrota, Dr. Nye received her medical degree from the University of Minnesota in 1914, the only woman in her class.

She has been the recipient of many honors including the University of Minnesota's outstanding achievement award. She held a life membership in the American Academy of General Practice, the first person to be so honored. For many years she was director of the St. Paul Bureau of Health Immunization Clinic and its part time medical ex-

aminer. Dr. Nye was also a former medical examiner for girls for the Ramsey County Juvenile Court, a physician for Welcome Hall Day Nursery and a staff member of the Amherst H. Wilder Foundation Dispensary. She was an honorary staff member of Miller, St. Luke's and Bethesda Hospitals and was cited by the Greater United Fund and Council, Inc. for outstanding service "in planning for human needs."

Dr. Nye was a member of the Ramsey County Medical Society and American Medical Association and a Life Member and 50 Club Member of the Minnesota State Medical Association.

She is survived by her sister, Dr. Lillian Nye of St. Paul, and a brother.

ELWYN R. BRAY, M.D.

Dr. Elwyn R. Bray, 88, retired St. Paul physician and surgeon, died March 19. He was born in Young America and lived in St. Paul fifty years. He retired from active practice in 1964.

Graduating from the University of Minnesota Medical School in 1901, he trained in eye specialization in London and Vienna. He was a member of the Ramsey County Medical Society, the American College of Surgeons, the American Academy of Ophthalmology and Otolaryngology, the American Medical Association and a Life and 50 Club Member of the Minnesota State Medical Association.

He is survived by his wife, two daughters, and three sons, one of whom is Dr. William N. Bray of St. Paul.



THE S.S. HOPE is a floating medical center — a fully staffed and fully equipped modern hospital which is the vehicle by which Project HOPE fulfills its mission of carrying American medical treatment and training to foreign lands where such help is not only needed but wanted. Project HOPE is a nongovernmental, nonprofit organization which is financed solely by voluntary contributions from individuals and private enterprise of North America.

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Before prescribing, please consult complete product information, a summary of which follows:

Contraindications: Infants, patients with history of convulsive disorders, glaucoma or known hypersensitivity to drug.

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Side Effects: Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances, acute hyperexcited states, hallucinations); changes in EEG patterns during and after drug treatment. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms (convulsions, tremor, abdominal and muscle cramps, vomiting, sweating) similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.

Dosage—Adults: Mild to moderate psychoneurotic reactions, 2 to 5 mg b.i.d. or t.i.d.; severe psychoneurotic reactions, 5 to 10 mg t.i.d. or q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; muscle spasm with cerebral palsy or athetosis, 2 to 10 mg t.i.d. or q.i.d. *Geriatric patients:* 1 or 2 mg/day initially, increase gradually as needed and tolerated. (See Precautions)

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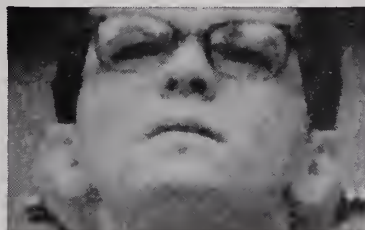


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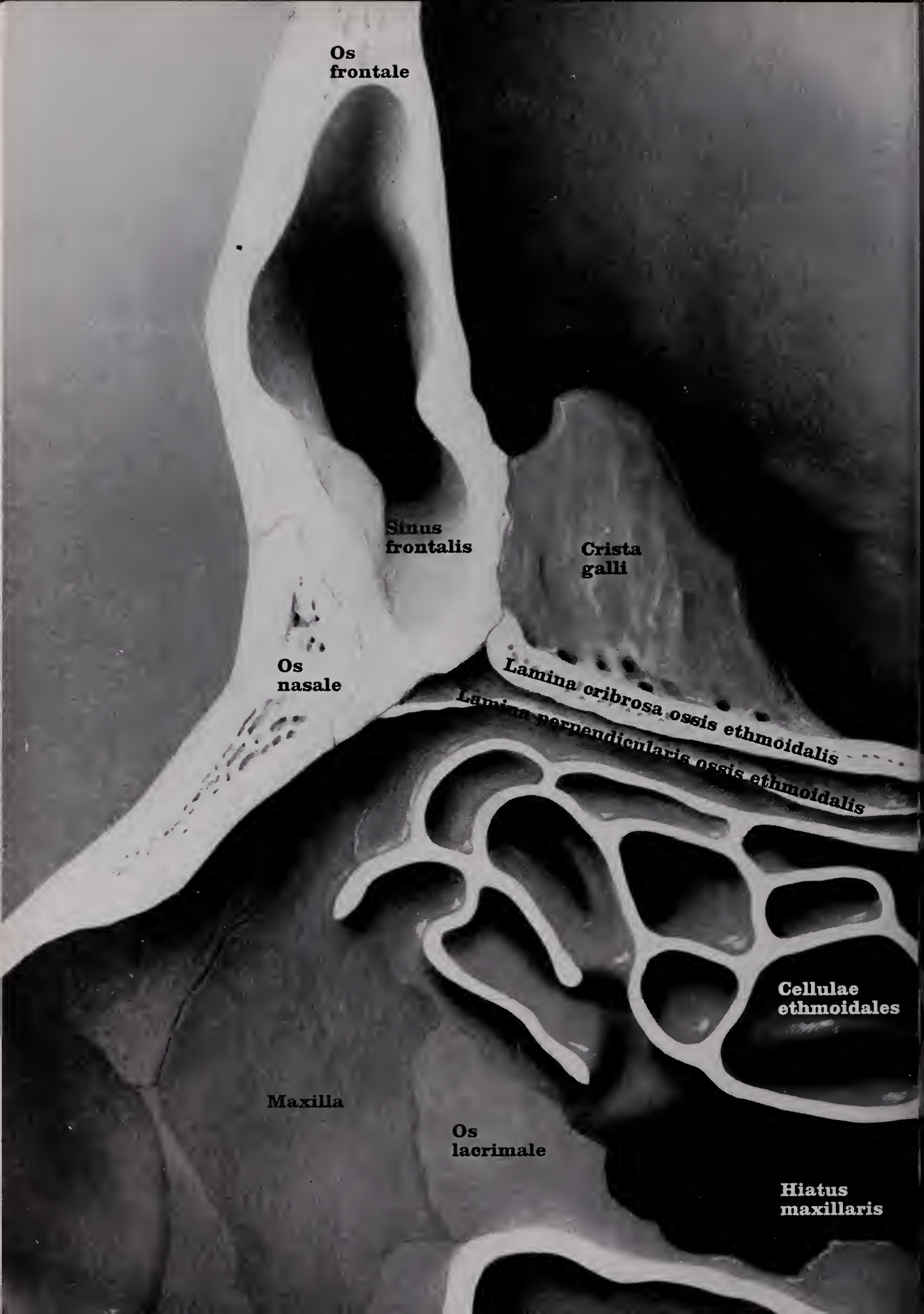
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WANTED: Young general practitioner to join five-man group consisting of three G.P.'s, a general surgeon, and radiologist. College town serving population of 22,000 30 miles from Twin Cities. Also need LOCUM TENENS in general practice. Contact: Ed Jenkins, Manager, River Falls Medical Clinic, River Falls, Wisconsin. Phone 425-5322

WANTED — Internist, board certified or qualified, to associate with two board certified internists. Ten man multi-specialty group. (Lenont Peterson Clinic, Virginia, Minnesota) — Heart of the expanding taconite industry.

WANTED: GP to join clinic serving population area of 12,000. City has new hospital, new clinic building, two nursing homes, new Jr-Sr high school, new swimming pool, rich farming area in Red River Valley. Fishing and hunting nearby; metropolitan city close by. Salary open and partnership if interested. Write or call Warren Clinic, Warren, Minnesota 742-6231, area code 218.

THREE MAN group in North West Wisconsin Resort, State Conservation and Retirement Area needs two more physicians adequately to serve their practice. Facilities offered are three-room physician suites, X-ray and lab under AMT technician, RN-only nursing personnel. New accredited thirty-two bed hospital and forty-six bed nursing home. Deer and duck hunting, fishing within five minutes of town. Internist most needed; generalists welcomed. Will meet any reasonable salary request. Partnership after one year. Write: MINNESOTA MEDICINE — 365; 496 Lowry Medical Arts Building, St. Paul 55102.

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WANTED: young internist and pediatrician, board certified or eligible, to join five-man group consisting of three G.P.'s, a general surgeon and a radiologist. College town serving population of 22,000; thirty miles from Twin Cities. Salary open with early partnership opportunity. Write or call collect: Ed Jenkins, Manager, River Falls Medical Clinic, River Falls, Wisc. Phone 425-5322.

GENERAL PRACTITIONER wanted to join well-established practitioner. New clinic building — 90 miles east of St. Paul — city of 14,000. Early partnership with full hospital facilities. Ideal location. L. W. Picotte, M.D.; Chippewa Falls, Wisconsin.

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INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE — 289; 496 Lowry Medical Arts Building; St. Paul, 55102.

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Continued on page 796



Meetings and Announcements

No one is likely to remember what is entirely uninteresting to him.

— G. MacDonald

MAY

Minnesota State Medical Association Annual Meeting, May 15-16-17, Duluth Civic Auditorium, Duluth, Minnesota.

Hennepin County Medical Society Membership Meeting, May 1, Pick-Nicollet Hotel, Minneapolis, 6:00 P.M.

Southwestern Minnesota Medical Society Meeting, May 1, Worthington, 7:00 P.M.

Scott-Carver County Medical Society Meeting, May 2, Wagner Supper Club, Jordan, 7:30 P.M.

Zumbro Valley Medical Society Meeting, May 3, Plummer Hall, Rochester, 7:00 P.M.

Minnesota Academy of Medicine Monthly Meeting, May 11, Town & Country Club, St. Paul, 6:30 P.M.

St. Louis County Medical Society Meeting, May 11, Executive Committee — 6:00 P.M., St. Mary's Hospital. Regular Meeting — 8:00 P.M., St. Mary's Hospital.

Minnesota Society of Internal Medicine Meeting, May 20, Minneapolis, 9:00 A.M.

Range Medical Society Executive & General Meeting, May 23, Place not determined, 6:00 P.M.

JUNE

A continuation course in Clinical Electroencephalography, June 5-7, Philadelphia, Pa. Sponsored by the American EEG Society and is designed for physicians who have had little or no formal EEG training. Inquiries address to: Donald W. Klass, EEG Course Director, Mayo Clinic, Rochester, Minnesota.

Southwestern Minnesota Medical Society, June 5, Worthington, 7:00 P.M.

Scott-Carver County Medical Society, June 6, Wagner Supper Club, Jordan, 7:30 P.M.

St. Louis County Medical Society, June 8, Executive Committee — 6:00 P.M., St. Luke's Hospital. Regular Meeting — 8:00 P.M., St. Luke's Hospital.

American Proctologic Society, Statler Hilton, Boston, June 15-18. Adminis Sec: James A. Ferguson, M.D., 320 W. Lafayette, Detroit 48226.

Flying Physicians Association, Lake Placid Club, Lake Placid, N. Y., June 15-20. Exec. Secy. Albert Carriere, 332 S. Michigan Ave., Chicago, Ill. 60604.

Idaho State Medical Association, [E], The Lodge, Sun Valley, June 25-28. Exec Sec: Armand L. Bird, 358 Sonna Bldg., Boise.

Society of Nuclear Medicine, New Orleans, June 25-28. Adm: Samuel N. Turiel, 333 N. Michigan Ave., Chicago 60601.

Society for Surgery of the Alimentary Tract, Barbizon Plaza, New York, June 21-29. Exec Sec: John Van Prohaska, M.D., 950 E. 59th St., Chicago 60637.

American Medical Association 116th Annual Convention, Atlantic City, New Jersey, June 18-22. Contact: AMA.

JULY

American Veterinary Medical Association, [E], Minneapolis, July 13-17. Act Exec Secy: D. A. Price, D.V.M., American Veterinary Medical Association, 600 S. Michigan Ave., Chicago 60605.

AUGUST

American Academy of Physical Medicine & Rehabilitation, [E], Sherman House, Chicago, Aug. 17-22. Exec Dir: Creston C. Herold, 30 N. Michigan Ave., Chicago 60602.

American Congress of Physical Medicine & Rehabilitation, Chicago, Aug. 17-22. Exec Dir: Creston C. Herold, 30 N. Michigan Ave., Chicago 60602.

International Biophysics Congress, Third, Boston, Mass., Aug 29-Sept. 3. Info: Dr. Walter Rosenblith, Center of Communication Sciences, Room 20B-221, Massachusetts Institute of Technology, Cambridge 02139.

National Medical Association, San Francisco, Aug. 11. Exec Sec: Samuel C. Smith, 520 W St., NW, Washington, D. C. 20001.

Wyoming State Medical Society, Jackson Lake Lodge, Moran, Aug. 26-29. Exec Sec: Arthur R. Abbey, P.O. Box 2266, Cheyenne 82001.

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BEAUTIFUL NEW OFFICE available now for second office or solo practice. Wonderful opportunity, progressive area, only specialists in area now are OB-GYN. Excellent lease arrangement! Write: MINNESOTA MEDICINE — 375; 496 Lowry Medical Arts Bldg., St. Paul 55102.

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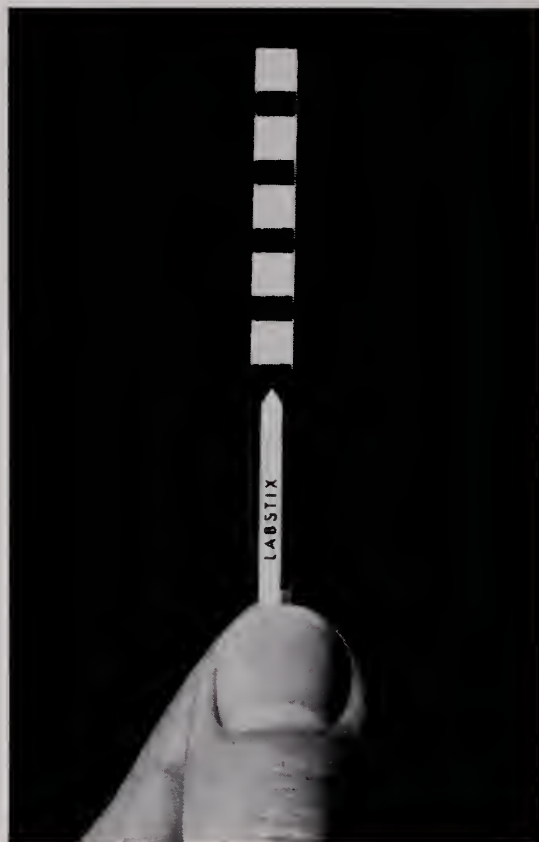
WANTED: GP to take over practice due to health. Equipment and all available with good financing. Northwest Suburban Minneapolis. Call or write: Bernard S. Nauth, M.D., 6120 Osseo Road, Minneapolis, Minnesota 55429. Phone: 561-4390 or residence 929-0958.

GENERAL PRACTITIONER wanted to join well established practitioner. Located 65 miles north of Minneapolis-St. Paul area. Population over 3,000. Hospital in town. Good schools, churches, and fine fishing and recreational area. Contact: A. C. Peterson, M.D., 200 E. Forest St., Mora, Minnesota 55051.

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LOCUM TENENS: Want Minnesota licensed G.P. to take over practice for June, July, August. Living accommodations, excellent salary. Write: MINNESOTA MEDICINE — 376; 496 Lowry Medical Arts Building, St. Paul 55102.



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WANTED: General surgeon to associate with six-man group. Progressive Northern Minnesota Junior College Town. Modern 150 bed hospital. Excellent hunting and fishing. Near metropolitan area. Contact: Falls-Starekow Clinic, Thief River Falls, Minnesota.

GENERAL PRACTITIONER WANTED: To associate with physician-surgeon in Owatonna, a Southern Minnesota community, 25,000 population. Clinic building three years old; with five large treatment rooms; lab; x-ray; central supply; two doctors' offices; pharmacy; and business offices. Located next door to 85 bed hospital. Good opportunity for partnership. Contact: O. W. Roberts, M.D., 920 South Cedar Street, Owatonna, Phone 451-4630.

WANTED LOCUM TENENS: Three-man Minneapolis GP group desires physician with Minnesota license to work during July, 1967. Salary and conditions excellent. Contact: 529-9251, Minneapolis.

GENERAL PRACTITIONER urgently needed to take over my very active practice on or before June 1, 1967. All equipment nearly new. Records extremely complete. Write: Gerald E. Cotton, M.D., Fosston, Minnesota.

WANTED: two general practitioners to join well established two-man group. Practice general surgery, medicine and O.B. Community Hospital, local clinic. 60 miles north of Twin Cities. Salary and working conditions to be discussed personally, Wm. T. Nygren, M.D., Braham Clinic, Braham, Minnesota. Phone 396-3355 office, 396-2153 residence.

EXCELLENT OPPORTUNITY established General Practice sixteen years. Country home, office, equipment available July 1. South Central Minnesota town 12,000. Specializing. Contact A. L. Ourada, M.D., Fairmont, Minnesota. Phone 235-5848.

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Physician's Diary

Nothing costs less, nor is cheaper, than the compliments of civility. — Cervantes

J. A. Cosgriff, Sr., M.D. of Olivia is the newly-elected president of the Association of American Physicians and Surgeons.

* * *

Dr. Marjorie J. Williams, Director of the Veterans Administration's Pathology and Allied Sciences Service, was recently awarded the coveted Federal Woman's Award. This award is granted annually to the top six career women in government.

* * *

Doctors William A. Piper of Mountain Lake, Einer Johnson of Bemidji, and Otto Bergan of Clinton have been nominated as candidates for "Minnesota's Outstanding Senior Citizen."

* * *

Doctors Kai Rehder, Sidney F. Phillips, William L. Furlow, Dennis M. Robertson, Hamlet A. Peterson and Paul H. Andreini have been appointed to the staff of the Mayo Clinic in Rochester.

* * *

NEW LOCATIONS . . . Dr. A. E. Sprafka, who has practiced medicine in Detroit Lakes since 1938, opened offices in Dilworth . . . Dr. Charles W. Roth has joined the Medical Block Clinic in Red Wing . . . Dr. Robert G. Carter has left Mora to take a residency in radiology at Swedish Hospital in Minneapolis . . . Dr. N. L. Gault, Jr., associate director of medicine and an associate dean of the University of Minnesota's medical school, has been named professor of medicine and associate dean for the internal program of the University of Hawaii Medical School . . . Dr. George M. Miks has joined the East Range Clinic in Aurora . . . Dr. Charles H. Bloom has joined the Hastings State Hospital's Medical staff . . . Dr. Warren Kleinhasser has left River's Edge Medical Clinic in Farmington to take a new position with the Minnesota Mutual Life Insurance Company . . . Dr. Dean E. Guenther has left his practice in West St. Paul for a position as civilian doctor with the U. S. Army's medical service.

* * *

Dr. Arnold S. Anderson is the new medical director of the Children's Hospital of Minneapolis, and Dr. I. T. Clark is the new chief of the medical staff of St. Mary's Hospital in Duluth.

Dr. T. G. Martens, consultant in ophthalmology in the Mayo Clinic, Rochester, has been elected chairman of the board of directors of Preschool Survey of Vision and Hearing and Dr. William H. Summer-skill, head of the Gastrointestinal Research Unit of the Mayo Clinic, has been made a fellow of the Royal College of Physicians of London.

* * *

Dr. R. R. Frear of Brooten is the new chief-of-staff of Glenwood Hospital in that community. Dr. G. E. Lee is the new vice president and Dr. B. A. Kolp, the new secretary-treasurer.

* * *

Dr. Waltman Walters, emeritus Mayo Clinic surgeon, has been appointed vice president of the Pan-Pacific Surgical Association.

Dr. Clayton Bennett of Rochester has been elected president of the Olmsted Community medical staff. Other officers elected were: Dr. Frank Sander, president-elect, and Dr. Fred Banfield, secretary-treasurer.

* * *

Doctors Jerome L. Kremer of Montevideo, James Kvale of Atwater, and Thomas Birkey of Montevideo have been elected to the American Academy of General Practice.

* * *

AMA — Dr. Don G. Mosser of Minneapolis has been reappointed a member of the Committee on Medicine and Religion . . . Dr. Francis W. Lynch of St. Paul has been reappointed a member of the Committee on Cutaneous Health and Cosmetics . . . Dr. George B. Logan of Rochester has been reappointed the principal representative of the American Academy of Pediatrics . . . Dr. Joe R. Brown of Rochester has been reappointed the principal representative of the American Academy of Neurology . . . Dr. Jan H. Tillisch of Rochester has been reappointed a member of the Council on Occupational Health . . . Dr. James C. Cain of Rochester has been reappointed a member of the Council on National Security.

* * *

Dr. Chris N. Christu of Moorhead has been named Seventh District representative on the Minnesota Liaison and Facilities Commission for Higher Education, an appointment made by the Governor.

* * *

The new officers for the Blue Earth County Medical Society are: Dr. Robert Conley of Mankato, chairman, Dr. John Heimark of Mankato, vice chairman and Dr. B. Niles Batdorf of Mankato, secretary-treasurer.

* * *

Dr. Anthony Spagnolo of Shakopee is the new chief-of-staff of the St. Francis Hospital in that city. Dr. James Ponterio was named new vice chief of staff with Dr. Richard Olson of Chaska named secretary-treasurer.

* * *

John Frederic Zurek, University of Minnesota medical student, has been awarded a foreign fellowship at the Holy Cross Hospital in Quilon-Kerala, India made possible by a grant from Smith Kline & French Laboratories.

* * *

Dr. V. D. Thysell of Moorhead is the new president of the Heart of the Lakes Chapter of the Minnesota Academy of General Practice. Dr. Glenn Brown of Halstad is vice-president; Dr. Olga H. Johnson of Moorhead, secretary-treasurer and Dr. John Holten of Moorhead, director.

* * *

Dr. John Rutledge of Detroit Lakes has received an award for his participation in raising the health status of the Indian population of the White Earth Reservation. The award is presented by the U. S. Department of Health, Education and Welfare, Bureau of Medical Services, Division of Indian Health.

Minnesota Medicine at a Glance

Erythrocyte Sedimentation Rate — Spellacy et al

Page 645

Two commonly used oral contraceptive drugs, one of the combined and the other of the sequential type, are shown in controlled studies to have an elevating effect on the erythrocyte sedimentation rate. The mechanism responsible for this elevation is probably similar to that in pregnancy. Clinicians are cautioned to consider this effect in the interpretation of the erythrocyte sedimentation rate result in women who are taking oral contraceptive drugs.

The Disturbed Patient? — Babb and Steinhilber

Page 649

This is a pertinent discussion of difficulties in patient-physician relationships. Distressing aspects of behavior in two patients are described and evaluated in light of the adverse effect upon the clinical course that is provided by pejorative labeling and hostile attitudes promoted by the physician in charge and supported by ancillary medical personnel. Remedial effects of a more open, honest, direct attitude affording improved communication and transactions are described. Attention to the concept of this paper will lead to increased patient comfort and response to therapy as well as to increased physician (and other medical personnel) comfort and effectiveness.

Fluorescence — Peterson

Page 663

Fluorescence techniques are receiving wide attention in the diagnosis of diseases associated with altered immune mechanisms. The author briefly reviews the basic principles and techniques involved in studying tissue fluorescence. The use of acridine orange and tetracycline fluorescence in the diagnosis of malignant tumors is discussed. The complexity of the methods and the questionable specificity of the results are the main problems in the application of these techniques in clinical situations. However, the clinician should have some familiarity with the methodology, since with further study and development, fluorescent antibody tests may become important means for diagnosis of a large variety of diseases.

Dr. L. K. Onsgard of Houston, Minnesota, mailed a television set to his son in the service for his birthday. The Postmaster told him that for fifty cents more they would give it "Special Handling." To this the Doctor agreed and stated, "The next time you need a shot, for fifty cents more I will use a sharp needle."

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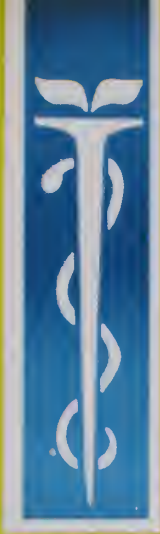
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JUNE, 1967

vol. 50 #6

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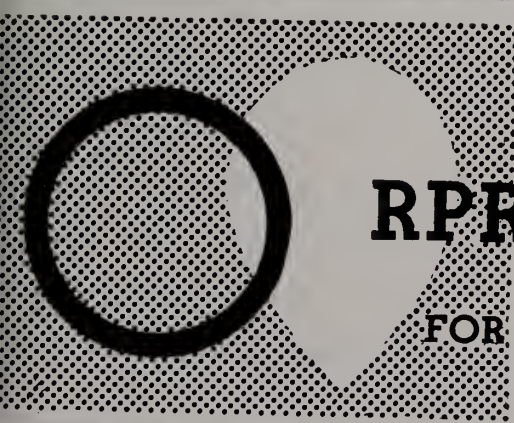
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Current Attitudes in Otolaryngology

Doctor Lawrence Randall Boies will retire as Chairman of the Department of Otolaryngology of the University of Minnesota Medical School on July 1, 1967. In recognition of this occasion and to honor this leader in American Otolaryngology, internationally-known authorities in the field have contributed their views on "Current Attitudes in Otolaryngology." They dedicate their efforts in this Tribute Edition of MINNESOTA MEDICINE to Lawrence Randall Boies, M.D. — friend and most respected confrere.

Volume 50

Number 6

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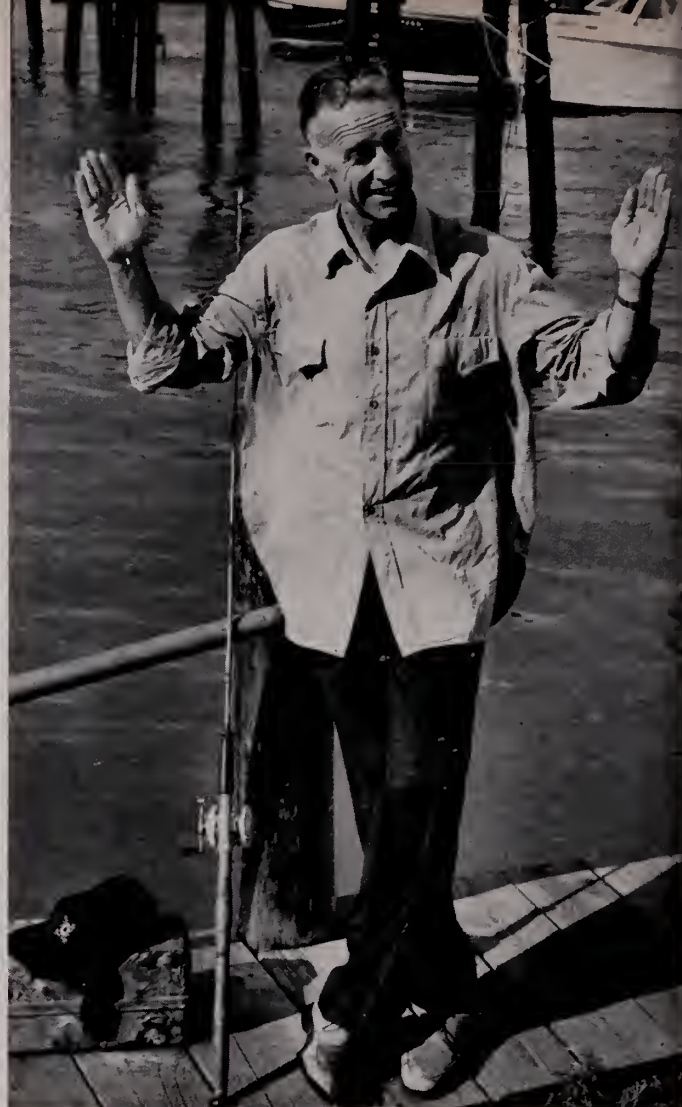
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President's Letter

THIS TIME I am really concerned. Since the advent of Medicare, there is developing a shortage of material for teaching purposes at the University of Minnesota Medical School. The patient who might formerly have been sent to the University Hospital is now being largely cared for in one of the many private hospitals in the state. This may be fine for the patients, but it is hard on the medical-school teaching staff.

It would seem to me that in this situation two birds might very well be killed with a single stone, as it were. The people of this entire country are faced with an acute shortage of family-doctor-type care. Recently there have been a spate of studies and reports, such as the Millis Report, the Health Manpower for Upper Midwest Report, and several other well-known studies on the same subject. All of them, without exception, have stressed the fact that there is a crucial need for not only more physicians, but especially more family physicians.

It is true that the ratio of physicians to population has increased over the past twenty years, but fewer doctors are going into private practice and more into research and other branches of medicine, which all adds up to a shortage of general practitioners. It seems to me that members of the private practice sector, as well as those on the University Medical School Faculty, could very profitably sit down together to work out mutual problems.

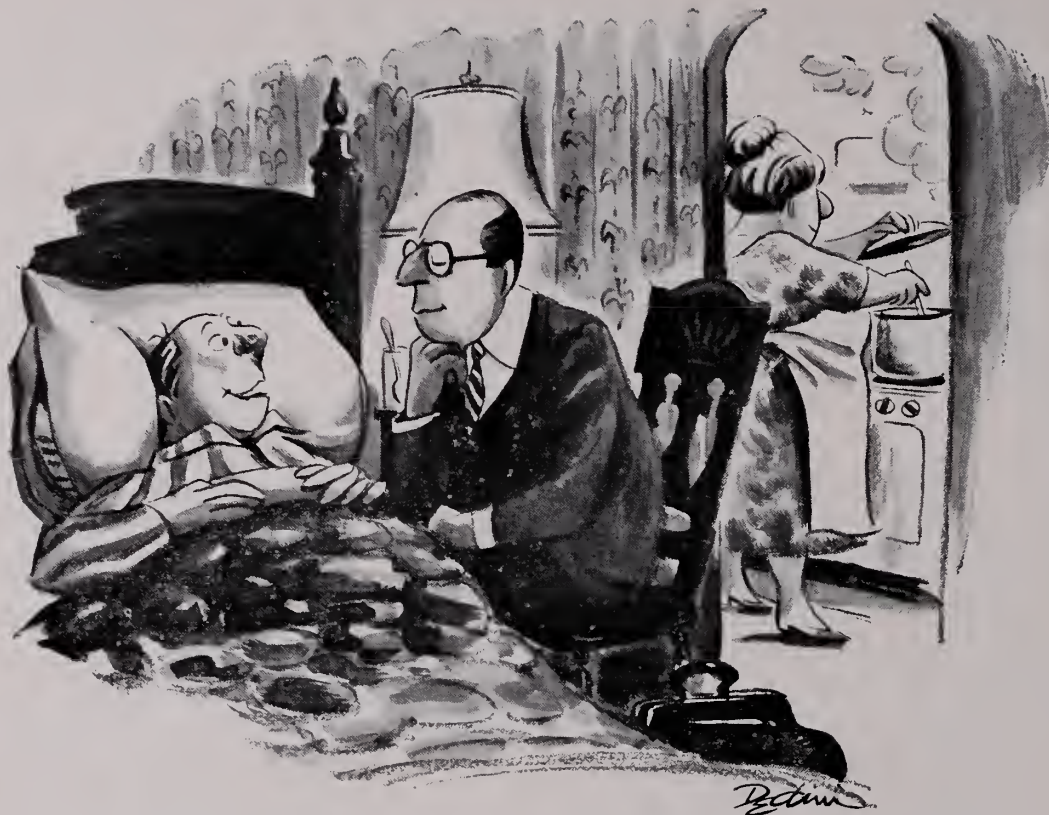
There are some faculty members who are enthusiastic about the production of greater numbers of family physicians; the great majority do, however, not appear to share

this enthusiasm. One thing is certain: more family physicians cannot be obtained from among the medical students by bribing, buying, or pushing them into this type of practice. They have to *want to go into it*. There must be motivation.

It would be my hope that the faculty could be so aware of their responsibilities to the people of this state that they would be eager to help motivate any of the students who showed an inclination for family practice, and that we could also enlist the volunteer assistance of that large group of residents in all fields of medical specialties, who have considerable association with and influence on the students. Is this expecting too much? Maybe so, but we hope the effort will be made. One of the most powerful motivations is precept, a method which has already been operating for years to induce students to go into specialty and research fields. So why not now partially reverse a hitherto successful procedure and urge more young doctors into family practice rather than into specialization.

I should like to suggest one way for increasing the number of patients entering the University Hospital for care and at the same time for providing a great deal more exposure to family type practice. It could be fairly easily determined how many family physicians would be required to provide sufficient referrals to the various departments within the medical school, so that sufficient teaching material could always be on hand. At least a start could be made toward developing a fairly steady supply of patients; and there would probably always be additional cases

Continued to page 1024



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Editorials



Lawrence Randall Boies, M.D.

DOCTOR LAWRENCE RANDALL BOIES has occupied the pivotal position in Otolaryngology in the North Central United States for the past twenty-five years.

"Chance favors the prepared mind," and the quickened pace of medical progress in the past thirty-five years found Otolaryngology in this geographic area blessed by the presence of this one-man "steering committee." Organization and administration are a subtle art form to him. He accomplishes a great deal because he is not particularly concerned about credit as long as the work is done.

The history of the University of Minnesota Medical School currently in preparation will note that Lawrence R. Boies, M.A., M.D., was born in Renville, Minnesota, in 1898. He graduated from the St. Croix Falls High School in 1915 and entered the University of Wisconsin. His studies were interrupted by World War I when he served as a corpsman in the Medical Corps of the U. S. Army. Returning to the University of Wisconsin, he received a B.A. degree in 1922 and an M.A. degree in 1923 while the first two years of the medical course were being completed. In 1923-24 he taught for a year in the High School in Pipestone, Minnesota, and then entered the College of Physicians and Surgeons of Columbia University where he received an M.D. degree in 1926. After internship and nineteen months of practice as an assistant to a general surgeon in Minneapolis, he enrolled as a graduate student at Harvard Medical School. This period, including a residency at the Massachusetts Eye and Ear Infirmary, covered a period of twenty-five months.

Doctor Boies' great fortune came to him in 1928 when he married Louise Marty. They have had three sons: Doctor Lawrence R. Boies, Jr., Clinical Instructor in Otolaryngology at the University of Minnesota School of Medicine, who divides his professional time between instruction, research and the private practice of Otolaryngology in Minneapolis; David, a Yale Law School graduate, associated with the First Trust Company of Minneapolis; and William (deceased).

Doctor Boies was first appointed to the University of Minnesota Medical School faculty in 1931 shortly after he established a private practice in Otolaryngology in Minneapolis. He continued in private practice in Minneapolis until 1955, when he became the first full-time head of Otolaryngology at Minnesota.

Doctor Boies had been appointed Clinical Professor of Otolaryngology and Director of the Division of Otolaryngology in 1942 following the resignation of Doctor Horace Newhart because of ill health.

In 1943, subsequent to the resignation of Doctor Frank Burch, Doctor Boies was appointed Chairman of the Department of Ophthalmology and Otolaryngology. He worked toward the establishment of Ophthalmology and Otolaryngology as separate Departments. This could not be accomplished until funds, space and full-time leadership in Ophthalmology became available in 1955.

Doctor Boies' leadership qualities are evident in the positions of honor he has held in the local medical societies and the major scientific societies of American Otolaryngology:

Minneapolis Academy of Medicine (President, 1934).

Hennepin County Medical Society (President, 1944).

Minnesota Academy of Medicine.

Minnesota Academy of Ophthalmology and Otolaryngology (President, 1944).

Minnesota State Medical Association (Chairman, Committee on Conservation of Hearing, 1942-1952).

American Medical Association (Chairman, Section L.O.R., 1960-61).

American Academy of Ophthalmology and Otolaryngology (Board of Secretaries 1947-1956; President, 1962).

American Laryngological, Rhinological and Otological Society, Inc. (Vice President, 1946; President, 1957).

American Laryngological Association (First Vice President, 1966).

American Otological Society (Secretary-Treasurer 1956-1960; Vice President, 1961; President, 1962).

Board of Trustees, Central Bureau of Research 1951 to date.

American Broncho-Esophagological Society.

American Board of Otolaryngology (Director 1948 to date; President 1962 to date).

Fellow American College of Surgeons.

He is the author of more than seventy papers published in various journals, textbooks, etc. Along with faculty colleagues he is also the author of a textbook "Fundamentals of Otolaryngology," now in its fourth edition.

His public service includes service on the Special Medical Advisory Board to the Veterans Administration 1953-1957; the Communicative Disorders Research Training Committee of the United States Public Health Service, National Institutes of Health, and currently he is on the National Institutes of Health Communicative Sciences Study Section, Division of Research Grants,

of which he is Chairman.

Parallel with all general and special medicine, Otolaryngology has progressed and changed in the past twenty-five years. Participation in these changes has been an exciting adventure for the staff associates who have shared the years with Lawrence Boies. They find comfort that his "retirement" is in reality only a change of scene and perhaps of pace but not a dissociation from the medical arena he has enlivened these many decades. Doctor Boies retires as Director of the Department of Otolaryngology of the University of Minnesota School of Medicine and assumes comparable responsibilities as Executive Director of the Deafness Research Foundation headquartered in New York. A second career of service lies ahead.

Jerome A. Hilger, M.D.
Guest Editor
St. Paul, Minnesota

The Editor's Soliloquy

Homage

To the honor of the dedicatee of this issue MINNESOTA MEDICINE has introduced a deviation from its routine format in order to include manuscripts from a long list of willing and competent contributors.

Perhaps this is a unique innovation in medical journalism, and to that extent it is probably justifiable to ask: What do we want from the medical publications we pay for?

From our State Society do we want a journal of medical economics that teaches us how to build volume, collect bills, make investments, plan insurance? Or do we prefer a scholarly publication that will maintain and enhance our prestige.

Do we want our modern medicine in 60-second abbreviated abstracts embalmed between pages of distracting advertisements that offer too much volume and too little value? Or do we want a learned periodical which permits us to share vicariously the valuable experience of colleagues who have devoted clinical acumen to specific medical and surgical problems?

Do we want a bulletin that will provide us with details about meetings, with personality trivia included? Or do we want an erudite journal that will reaffirm and fortify our professional image as up-to-date practitioners, conversant with the current well documented literature.

Because it is believed that most of our readers want the latter of these several choices, MINNESOTA MEDICINE is herewith offering, not a complete list of vital statistics pertaining to the dedicatee, but rather an aggregate of monographs contributed by admiring and eager authors who welcome an opportunity to pay homage to their retiring chief.

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Basic Research Contributions to Otology

MERLE LAWRENCE, Ph.D.*
Ann Arbor, Michigan

PROBABLY NO OTHER advance in Otology reflects the contributions of basic science more than surgery for deafness due to otosclerosis and for deafness due to chronic, eroding infections of the mastoid and middle ear. There are those today who maintain that basic science had nothing to do with the success of these procedures, that this is the result only of the insight of adventurous surgeons, but this is because these surgeons have knowledge they take for granted and do not realize the struggle that once took place to establish these seemingly obvious facts. So before the surgeons of the future become thoroughly imbued with the notion that it is their own courageous spirit that makes advances, it would seem appropriate to review some of these early contributions.

It was not always known that aerial vibrations were involved in the production and transfer of sound and, although air as a medium in which we live has "forever" been recognized, it has been only within the last three hundred years that air was definitely established as the necessary medium for the transfer of sound. And before any true knowledge of how the ear operates could be obtained, the characteristics of sound in air had to be discovered.

Galileo (1564-1642), often called the founder of modern physics, turned some of his ingenuity to the study of vibration and arrived at the significant conclusion that the important factor in determining pitch is the number of vibrations per unit time. He apparently arrived at this conclusion by an experiment in which he scratched a brass plate with an iron chisel. When the scraping produced a high-pitched note the intermittent scratches appeared close together while a low-pitched note produced marks farther apart. The manner in which vibration involved air in traveling through space was apparently very obvious to him. In his *Dialogues* he says: "Waves are produced by vi-

*Professor of Otorhinolaryngology and Physiology, University of Michigan Medical School and Director, Kresge Hearing Research Institute.

brations of a sonorous body, which spread through the air, bringing to the tympanum of the ear a stimulus which the ear interprets as sound." But still, this had not been proven by experiment, and so the issue was not really settled despite the respected authority of Galileo.

The Nature of Sound

It remained for two students of Galileo to find a way to produce a vacuum. In 1644 Evangelista Torricelli (1608-1647) reported his invention of the barometer. He died just three years after this brilliant demonstration, but another student, Viviani, carried on the experiments with new devices. Experiments in creating a vacuum were not taking place in Italy alone, however; an entirely different method was being employed by the Burgomaster of Magdeburg in Germany, Otto von Guericke (1602-1686). Von Guericke made the first air pump and performed the famous demonstration of the Magdeburg hemispheres.

Once air could be removed from a space it was possible to test the necessity for air in the transmission of vibrations. Such experiments were quickly performed and differed depending upon whether the vacuum was created by a Torricellian barometer or a von Guericke air pump.

In 1650 the Jesuit, Father Kircher (1602-1680), reported the first recorded experiment involving the sounding of a bell in a Torricellian vacuum. The bell was heard because, as we know now, the vibrations were carried along the supporting bar, and Father Kircher therefore concluded that air is not necessary for the transmission of sound. The problem was clouded still further when in 1657 the Accademia Del Cimento of Florence repeated Kircher's experiment and came to the same conclusion. Facts in science do not come easy!

It remained for Robert Boyle (1627-1691) to perform the crucial experiment in 1660. He evacuated a bell jar by means of an air pump and demonstrated that, with proper isolation of the bell, the sound did not travel through a vacuum. Subsequent experimentation led to the disclosure of the law

(Boyle's law) that the volume of a gas is inversely proportional to the pressure.

From this time on, experiments with sound took on real meaning. Measurements of the speed of propagation of sound in air, solids, and water were made, but the first serious attempt to theorize about the nature of sound was made by Sir Isaac Newton (1642-1727). He proposed a wave theory and described the propagation of sound as a series of pulses produced by the vibrating body. These pulses in the medium produce further pulses in adjacent positions of the surrounding medium and so the vibration moves outward away from the source. Thus the era of understanding the mechanical nature of sound began, and the voluminous research that followed has brought us to the concepts we have today that help clarify the acoustico-mechanical properties of the ear.

Auditory Physiology

While the physicists were debating and experimenting, the anatomists were slowly bringing to light the auditory structures that respond to air-borne vibrations. In 1777 Philipus Fridericus Meckel (1756-1803) furnished proof for the statement of Domenico Cotugno (1736-1822) that the inner ear contains fluid, not air, as had long been the belief. Meckel simply opened, under water, the inner ears of some cats and saw no escaping air bubbles, an observation that supported his earlier observation that frozen human inner ears contained ice crystals. It remained for such brilliant anatomists as Huschke, (1797-1858), Corti (1822-1876), and Retzius (1842-1919) to describe the fine structures of the inner ear and later for Wever and Bray¹ to record the electrical potentials that provided a powerful technique for the study of auditory physiology.

The Ossicular Chain

Although it seems so obvious today, the mechanical properties of the middle ear have been almost as difficult to elucidate as were those of air-borne vibrations. In 1683 Joseph Guichard DuVerney² (1648-1730) suggested that the round window might be an important route for the entrance of sound into

the inner ear, although he also recognized that the role of the ossicular chain is probably more important. The question was resolved, but still debated for over a hundred years, by the extraordinary German physiologist Johannes Müller (1801-1858), who numbered among his students the equally famous physiologist and physicist Hermann von Helmholtz (1821-1894). In his large handbook of physiology,³ published in 1840, Müller reports an experiment to demonstrate that vibrations are transmitted from air to a liquid much more effectively when a tense membrane and a chain of bones are the conducting media than when a tense membrane, air, and a second membrane conduct the vibrations. However, while this experiment demonstrated the important role of the ossicular chain, much further experimentation was necessary in order to demonstrate the role of the two windows in the ear and the mechanics of the membrane and chain of bones that enable them to be the most effective route.

Pressure Transformation

Many fine experiments must be skipped in this report, but certainly one of the most diligent investigators has been Georg von Békésy, winner of the 1961 Nobel prize in medicine and physiology (the first physicist to be awarded the prize in this category) for his work on the inner ear. Among many other experiments Békésy⁴ measured the over-all pressure transformation accomplished by the middle ear. A sound source was applied through a sealed conductor to the external meatus of a cadaver temporal bone and another source to the inner surface of the footplate of the stapes. The amplitude and phase of this latter source were adjusted until the effect of the two sounds, one through the tense membrane and chain of bones and the other at the footplate, immobilized the stapes. The ratio of the two pressures when the stapedia footplate remained at rest represents the pressure transformation of the middle ear which turned out to be a ratio of about 15 times.

Wever and Lawrence,⁵ by physiological means, considered the areal and lever ratios

in further detail. When Dahmann's⁶ figure for the lever effect of the peculiarly-arranged ossicular chain is added to the areal ratio between tympanic membrane and stapes footplate, the total advantage of the membrane and ossicular chain amounts to 25.5 dB, which is the amount of hearing loss to be expected as the result of a fenestration operation, or one in which the stapes remains after removal of the membrane and ossicular chain, and the round window protected.

The Era of Middle Ear Surgery

Surgery on the middle ear in cases of ankylosis of the stapes started in the final quarter of the last century based on the clinical observation, and on the knowledge furnished through experiment by Müller, that a freely mobile ossicular chain is necessary for normal hearing.

Surmounting Infection

Various degrees of success were achieved, not because of inconsistencies in the physical principles involved in the relay of sound to the inner ear, but because of subsequent infection and of the inability of the surgeon to visualize clearly the operative field. In 1928 the Scottish bacteriologist Sir Alexander Fleming (1881-1955) isolated the mold *Penicillium notatum* which exuded a substance capable of inhibiting bacterial growth. He called this substance penicillin but, being no chemist, he was unable to isolate or identify this substance further. Although the era of "wonder drugs" really began with the discovery of the bactericidal effects of the sulfa compounds in 1932 by Domagk (1895-1964), a German biochemist and winner of the Nobel Prize in 1939, the subsequent chemical isolation of penicillin by Florey and Chain, who shared the 1945 Nobel Prize with Fleming, and its successful use for war casualties in Tunisia and Sicily during World War II, introduced the age of the true antibiotics.

The Operating Microscope

The use of the microscope and the more recently developed antibiotics now make novel approaches to the surgical restoration

of hearing possible. However, the success of these procedures still depends upon practical knowledge of the mechanics and physiology of the ear, and the better schooled the surgeon is in these areas the greater his chances for successful advance of techniques.

Conclusions

We see today the bold onrush of surgeons to enter the realm of sensori-neural deafness. The activity is reminiscent of the late 19th century surgeons working in the middle ear. In the inner ear, however, we find different

problems; they are ones of hydrodynamics and biophysical chemistry. And we are today less advanced in our knowledge of this area than we were in our knowledge of middle ear mechanics at the time of Johannes Müller's experiments.

The same blundering paths may be followed, but certainly something could be learned from the past. A careful examination of the known facts and a concerted effort to fill in the gaps would be far more rewarding for surgical success than surgery first and a later guess at the basic mechanisms involved.

References

1. Wever, E. G. and Bray, C. W.: Auditory Nerve Impulses. *Science* 71:215, 1930, and Action Currents in the Auditory Nerve in Response to Acoustic Stimulation. *Proc Nat Acad Sci U S A* 16:344, 1930.
2. DuVerney, J. G.: *Traité de l'Organe de l'Ouïe*, Paris, 1683.
3. Müller, J.: *Handbuch der Physiologie Menschen* (J. Holscher: Coblenz, 1840), Vol. 2, Abt. 1. p. 393; Eng. transl. by W. Baly, *Elements of Physiology* (1842), p. 1215.
4. Békésy, G. v.: Über die Messung der Schwingungsamplitude der Gehörknöchelchen mittels einer kapazitiven Sonde. *Akust Zeits* 6:1, 1941.
5. Wever, E. G. and Lawrence, M.: *Physiological Acoustics*. (Princeton University Press, Princeton, New Jersey, 1954).
6. Dahmann, H.: Zur Physiologie des Hörens; Experimentelle Untersuchungen über die Mechanik der Gehörknöchelchenkette, sowie über deren Verhalten auf Ton und Luftdruck. *Z. Hals-Nasen- u. Ohrenheilk* 24:462, 1929; *ibid* 27:329, 1930.

Yes, I Will Be a Doctor

On a blistering day in early August something happened, and the whole course of my future life was changed.

The oats had been cut by the reaper the day before and lay in loose bundles on a side hill which sloped toward the west. Working alone, I crossed and recrossed the field, binding these oats. The straw was dry and did not impart the coolness peculiar to freshly cut grain. The heat was oppressive and fairly scorched my face as I leaned over these parched masses of straw. At the end of a row I stopped momentarily in the shade of a thorn bush which protected the black jug of drinking water. Not a breath of air was stirring; it was almost suffocating. There was no comfort except in the movement of the body. At three o'clock it became unbearable.

Bordering the field was a country road. At that particular location there were a number of large, hardwood maples whose deep, dark shade protected the wagon track. As I straightened up to wipe the flowing perspiration from my eyes with the sleeve of my shirt, I viewed a scene from paradise.

Driving leisurely along the road in the shade of the maples was Dr. Daniel McLaren Miller, then the famous family physician of Oconomowoc. He was dressed in white linen, his buggy had a white canvas top and open sides, and the horse was protected by a white fly net that extended over its whole body, even to its ears. Before my eyes was a picture that brought joy to my soul and envy to my mind.

Instantaneously I dropped my rake and gazed until the apparition leisurely passed out of sight around the bend in the road. "Yes, I will be a doctor. Why haven't I thought of it before?"*

*Franklin Martin (1857-1935) in *WHY WE BECAME DOCTORS*, edited by Noah Fabricant, 1954.

Surgery for Otosclerosis

HOWARD P. HOUSE, M.D.*
Los Angeles, California

THE HISTOPATHOLOGY of otosclerosis, or hardening of the ear bone, was described by Politzer¹ in 1887, as circumscribed bony protuberances that fixed the stapes in the oval window of the middle ear.

Historical

Meniere,² of vertigo fame, was the first to obtain temporary hearing improvement by manipulation of the ossicular chain. This was accomplished in 1842 by applying pressure on the malleus through the intact ear drum of a patient with probable otosclerosis.

Kessel,³ in 1894, was the first to perform mobilization and extraction of the stapes to improve deafness due to otosclerosis.

At the turn of the century, many otologists such as Boucheron,⁴ Miot,⁵ Moure,⁶ Passow,⁷ Blake⁸ and others were occupied in stapes surgery. Lack of adequate illumination and magnification hampered their ability to visualize the ossicular structures of the middle ear. Since antibiotics were unknown, otitis media and meningitis were rather common complications. Inasmuch as permanent hearing improvement was rare and the complications were severe, the surgery for otosclerosis by this method was largely abandoned.

Fenestration Operation

In the 1930s, surgery for otosclerosis was again revived by Sourdille⁹ of France and Holmgren¹⁰ of Sweden. The procedure developed by these men was known as the fenestration operation. Subsequently this operation was perfected by Lempert¹¹ of New York City. During the intervening years that followed the abandonment of stapes surgery, more accurate testing equipment (audiometers) became available. Improved

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From the Otologic Medical Group.

Sponsored by the Los Angeles Foundation of Otology.

illumination with the electric headlight and magnification with the two-power magnifying loop together with the introduction of sulfa drugs to control infection made more definitive otologic surgery possible. Lempert made use of all of these aids in perfecting his one-stage fenestration operation. This technique bypassed the fixed stapes by making a window in the horizontal canal of the labyrinth. The fenestration operation was a major surgical procedure requiring mastoid exposure, a week of hospitalization and two or three weeks of disability. However, it was successful in restoring permanent hearing in approximately 70 per cent of the cases.

Shambaugh, Jr. later introduced the Zeiss operating microscope to otologic surgery in the United States. This instrument is indispensable today in modern ear surgery.

The fenestration operation remained the accepted surgical procedure for the relief of otosclerotic deafness for some 20 years. In 1953, Dr. Samuel Rosen¹² of New York repopularized the stapes mobilization operation by applying modern instrumentarium to the previously abandoned stapes mobilization concept.

Although hearing could be improved by stapes mobilization in a high percentage of cases, this improvement was often of short duration due to regrowth of otosclerosis again refixing the stapes in the oval window area.

Stapedectomy

Recognizing that most of the otosclerotic regrowth involved the anterior portion of the stapes, Fowler, Jr.¹³ developed the anterior crurotomy procedure, which consisted of removing the anterior crus of the tiny stapes and mobilizing the posterior uninvolved portion of the stapes footplate. Although the operation was highly successful, the procedure was possible in only a small percentage of cases.

Shea¹⁴ attacked the problem by removing the entire stapes, placing a vein graft over the open oval window to seal the vestibule of the inner ear and establishing continuity with the incus by means of a polyethylene tube prosthesis. This procedure became

known as a stapedectomy and greatly enhanced the incidence of permanent hearing improvement. It soon became apparent, however, that slippage of the polyethylene tube would occasionally occur, sometimes with disastrous results if the tube entered the vestibule, thereby damaging the delicate inner ear structures.

To overcome the problem of polyethylene tube slippage, Hough¹⁵ devised the partial stapedectomy operation. In this procedure the anterior crus together with the anterior portion of the fixed footplate was removed, thereby allowing the posterior crus and the remaining uninvolved footplate to transmit the sound wave to the fluids of the inner ear. This procedure is in common use and is highly successful when fixation is limited to the anterior portion of the stapes footplate.

Schuknecht¹⁶ substituted a wire prosthesis for the polyethylene strut and used fat to cover the oval window area. Kos¹⁷ advocated wire and vein, and House²¹ wire and gelfoam.

The partial stapedectomy and the wire gelfoam technique are now widely accepted. Some surgeons (Shea,^{19,20} Guilford,¹⁸ McGee and others) use teflon or wire pistons as a stapes substitute and report very satisfactory results.

The Nature

Otosclerosis may be stapedial, involving only the stapes and oval window area (Figure 1); cochlear, involving only the inner ear mechanism (Figure 2); or both stapedial and cochlear. (Classification proposed by Shambaugh, Jr.).

The cause of otosclerosis is not known. The disease is hereditary, and patients with otosclerosis often have a positive family history of hearing impairment. Pregnancy seems to activate the progress of the disease in some cases. Otosclerosis involves both ears in some 80 per cent of the cases.

Diagnosis

Otosclerosis is characterized by a history of progressive hearing loss usually beginning in early adulthood and slowly progressing until the fifth or sixth decade when it seems to become more stationary. The hearing loss

usually progresses very slowly but at times may be quite rapid, especially during pregnancy.

The type of hearing loss is usually of a conductive or middle ear nature in its early stages; later the inner ear often becomes involved, thereby producing a mixed type of conductive and inner ear or sensori-neural impairment.

Loss of Low Tones

Characteristically the patient hears better in a noisy environment and tends to speak softly. This is typical of middle ear deafness since the low tones of noise are not heard as well as the higher tones of speech. Since the patient hears his own voice loudly, he compensates by speaking very softly. Chewing crunchy food such as celery or crackers sounds extremely loud to these patients; therefore their ability to hear is often greatly impaired at the dinner table. In this stage of the disease, the patient understands speech very well if adequate volume is presented. One can readily duplicate the dilemma of a patient with a conductive or middle ear type of hearing loss by simply plugging the ear canals.

Tinnitus

Tinnitus is common in patients with otosclerosis and may be most annoying. Again, the cause of this phenomenon is not known. Improvement in hearing either with a hearing aid or through surgery may diminish this symptom by simply producing more outside sound, which then tends to mask the patient's awareness of the "inside sounds."

Slight unsteadiness on motion may be elicited if careful inquiries are made of these otosclerotic patients. The instance of this symptom seems to be slightly higher in patients with otosclerosis than it is in the normal hearing individuals. Again the exact cause of this slight vertigo is not known.

As the inner ear becomes more involved, the patient tends to hear less well in a noisy environment and has more difficulty understanding speech even though adequate volume is presented.

Bone Conduction Better Than Air Conduction

The characteristic physical findings in otosclerosis is a perfectly normal ear and ear drum. Occasionally, one may observe a reddish hue due to increased vascularity. This finding is known as Schwartze's sign.

A 512 or 1024 tuning fork is heard better by bone conduction than by air conduction. Audiometric tests reveal a typical conductive or mixed type of pure tone audiogram. Speech tests reveal good ability to understand the spoken word when the volume is adequate.

The above tuning fork and audiometric tests are the typical responses of a patient with otosclerosis who has a conductive or even a mixed type of hearing impairment. As the inner ear becomes more involved, the tuning forks may become less definitive, the audiometer will reveal an inner ear or sensori-neural type of loss, and the speech tests will reveal decreased ability of the patient to understand the spoken word.

Conventional X-ray films may reveal sclerosis of the otic capsule. Laminagraphy or polytomography may reveal sclerosis involving the oval window niche and the stapes area.

Determination for Suitability for Surgery

The patient who is suitable for otosclerosis surgery is also suitable for a hearing aid. For either to give satisfactory hearing, the inner ear function must be reasonably good. If one cannot understand speech in spite of adequate amplification, it indicates excessive inner ear involvement and the patient is probably not suitable for surgery and will probably not accept a hearing aid.

Suitable Criteria for Surgery

1. He gives a history of progressive hearing loss of a conductive type: (a) he hears better in a noisy background; (b) crunchy food sounds loud to the patient; (c) he understands speech well when sufficient amplification is present.

2. He has a normal ear canal and ear drum.

3. He hears a 512 and preferably 1024

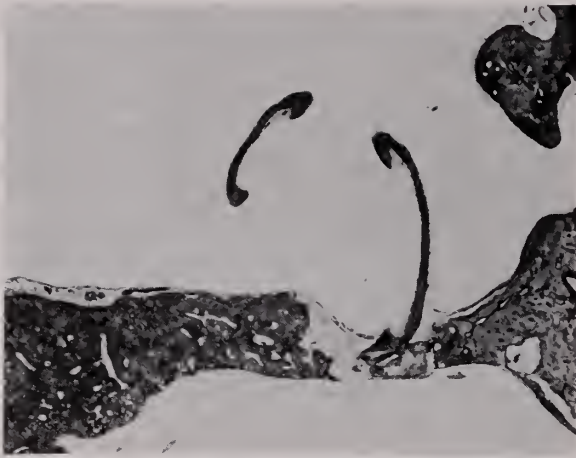


Fig. 1 — Temporal bone section illustrating stapedia otosclerosis. Note complete stapes footplate fixation.

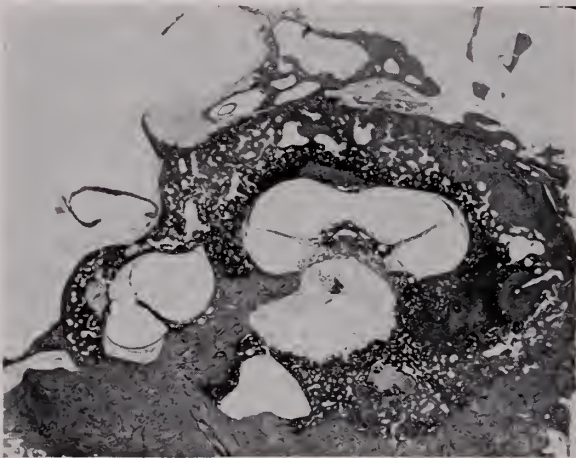


Fig. 2 — Cochlear otosclerotic bone completely encapsulating the cochlea of the inner ear.

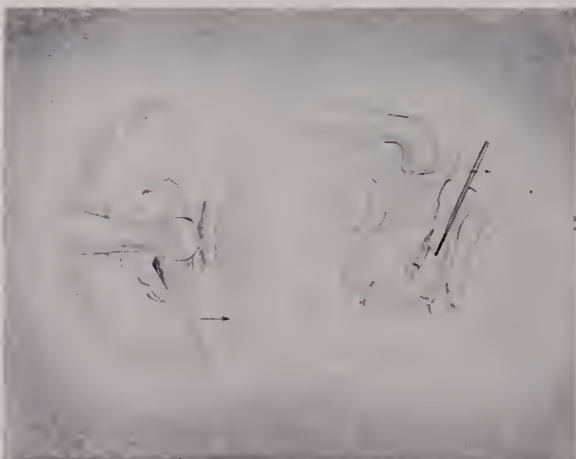


Fig. 3 — Fracturing the stapes crura.

tuning fork longer by bone conduction than by air conduction.

4. He has a conductive or middle ear type of pure tone audiogram.

5. He is in good physical health (age is not a contraindication).

Inner Ear Function

The extent of hearing improvement after surgery depends on the ability of the inner ear and hearing nerve to carry the sound to the brain. If the inner ear function is excellent, the patient may expect permanent restoration of serviceable hearing. If the inner ear function is moderately impaired, he may expect permanent restoration of serviceable hearing for near conversation but may need a hearing aid for distant communication. If the inner ear function is severely impaired, the hearing level may be permanently improved to allow better use of the patient's hearing aid (less volume and, therefore, less distortion). This type of improvement may also allow the patient to change from a body type of hearing aid to an ear level instrument. If the inner ear function is very severely impaired, the hearing level may be permanently improved sufficiently to allow the essentially deaf patient to hear some sounds with a strong hearing aid.

The degree of hearing improvement to be expected must be clearly explained to each patient depending on the amount of inner ear function that is present.

Surgical Technique

The operation is usually performed under local anesthesia and requires 20 to 40 minutes of operating time. The ear drum is elevated to expose the contents of the middle ear. The fixed stapes (Figure 1) is disarticulated from the incus, and the stapes together with the footplate is removed from the oval window (Figure 3 and 4) thereby exposing the perilymph in the vestibule of the inner ear. The oval window is covered with tissue or with gelfoam, and a prefabricated wire loop of proper length is placed in position and attached to the incus (Figure 5). A fibrotic membrane becomes enmeshed* in the wire and closes the oval window.

*See Test Your Word Score Page 1028.

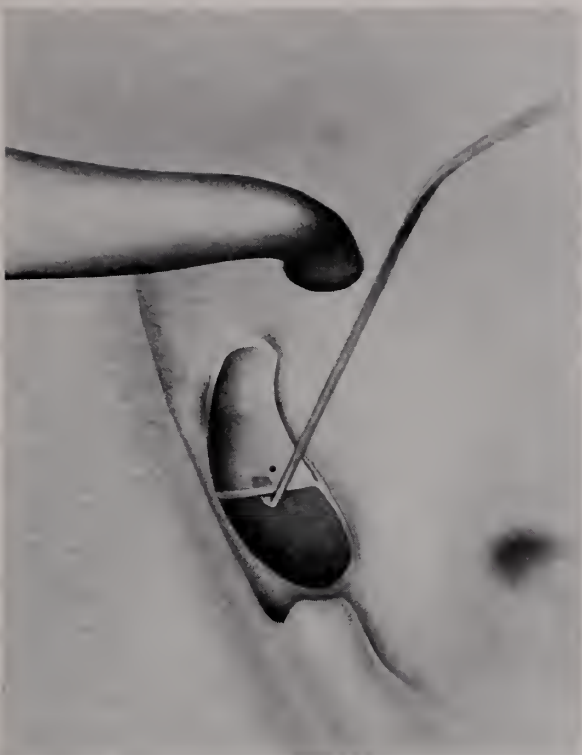


Fig. 4 — Removing the stapes footplate from the oval window exposing the vestibule of the inner ear.



Fig. 5 — Compressed gelfoam over the oval window and insertion of the prefabricated wire-loop.

Sound vibrations are then transmitted directly to the fluids of the inner ear through the wire and fibrotic membrane (Figure 6). The ear drum is replaced, and the patient usually leaves the hospital the following morning and may return to work a week or ten days later.

Prognosis

In general, permanent hearing improvement can be expected in 90 per cent of the cases operated. Two per cent may be worse following surgery, and the remainder are essentially unchanged or slightly improved.

Complications

Certain complications may occur during or following stapes surgery.

Otitis Media

Middle ear infection may occur in spite of prophylactic antibiotic therapy in some 2 per cent of the cases. Ear pain develops and the ear drum may rupture. Early and adequate treatment usually resolves this problem.

Ear Drum Perforation

Occasionally a perforation may occur either as a result of infection or due to surgical trauma. Fortunately these perforations usually heal spontaneously without sequelae. If the perforation does persist, the opening may be closed by grafting (myringoplasty).

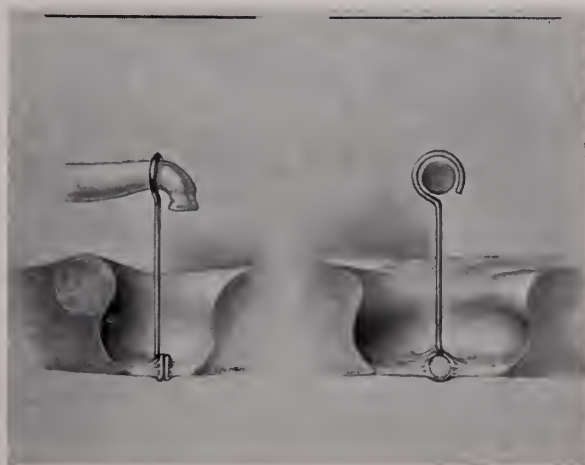


Fig. 6 — Reveals the prefabricated wire loop attached to the incus and enmeshed in the fibrotic membrane that covers the oval window.

Vertigo

Patients often have unsteadiness for several hours after surgery due to the opening of the vestibule of the inner ear. It is rare for this symptom to persist more than 24 hours. Occasionally some unsteadiness on sudden motion may be present for several months.

Further Hearing Loss

In 2 per cent of the cases operated and for reasons not clearly understood, the inner ear function may be impaired moderately or severely following stapes surgery. Because of this possibility, it is customary to operate on the poorer hearing ear.

Taste Disturbance

In some cases, an abnormal metallic taste may be present for several months after surgery, due to chorda-tympani nerve involvement.

Summary

The clinical diagnosis of otosclerosis is

References

1. Politzer, A.: Geschichte der Ohrenheilkunde. Stuttgart, Ferdinand Enke. Vol. 1, 1907; Vol. 2, 1913.
2. Meniere, P.: De l'Exploration de l'Appareil Auditif, ou Recherches sur les Moyens Propres a Conduire au Diagnostic des Maladies de l'Oreille. Gaz Med France, Vol. 10, 1842.
3. Kessel, J.: Ueber die vordere Tenotomie, Mobilisierung und Extraction des Steigbugels. Jena, G. Fischer, 1894.
4. Boucheron, E.: La mobilisation de l'Etrier. Bull Med Paris, 2:1225, 1888.
5. Miot, C.: De la mobilisation de l'etrier. Rev Laryng 10:49, 1890.
6. Moure, E. J.: De la mobilisation de l'etrier. Rev Laryng 7:225, 1880.
7. Passow, K. A.: Operative Anlegung Einer Offnung in die Mediale Paukenhohlenwand bei Stapes-ankylose. Verh Deutsch Otolaryng Ges 6:141, 1897.
8. Blake, C. J.: Operation for Removal of the Stapes. Boston Med Surg J 127:469, 1892.
9. Sourdille, M.: New Technique in the Surgical Treatment of Severe and Progressive Deafness from Otosclerosis. Bull N Y Acad Med 13:673, 1937.
10. Holmgren, G.: Some Experiences in Surgery of Otosclerosis. Acta Otolaryng 5:460, 1923.
11. Lempert, J.: Improvement in Hearing in Cases of Otosclerosis: A New, One Stage Surgical Technic. Arch Otolaryng 28:42, 1938.
12. Rosen, S.: Mobilization of the Stapes to Restore Hearing in Otosclerosis. New York J Med 53: 2650, 1953.
13. Fowler, E. P., Jr.: Anterior Crurotomy and Mobilization of the Ankylosed Stapes Footplate. Acta Otolaryng 46:318, 1957.
14. Shea, J., Jr.: Fenestration of the Oval Window. Ann Otol 67:932, 1958.
15. Hough, J. V. D.: Partial Stapedectomy. Ann Otol 69:571, 1960.
16. Schuknecht, H. F.: The Metal Prosthesis for Stapes Ankylosis. Arch Otolaryng 71:287, 1960.
17. Kos, C. M.: Personal Communication.
18. Guilford, F. R.: Stapedectomy Results with the Teflon-Wire Prosthesis. Laryngo 74:656, 1964.
19. Shea, Jr., J. J.: The Teflon Piston Operation for Otosclerosis. Laryngo 73:508, 1963.
20. Shea, Jr., J. J., Sanabria, F. and Smyth, G. D. L.: Teflon Piston Operation for Otosclerosis. Arch Otolaryng 76:516, 1962.
21. House, H. P.: The Prefabricated Wire Loop-Gelfoam Stapedectomy. Arch Otolaryng 76:298, 1962.

based on the history of a progressive, conductive type of hearing loss without evidence of other ear pathology to account for this symptom.

Suitability for surgery can often be determined by the simple use of tuning forks and the patient's ability to clearly understand amplified speech. More definitive audiologic tests are always indicated before positive selection of cases can be made.

The stapes operation now permanently improves hearing in 90 per cent of the cases operated. The degree of the improvement depends on the ability of the inner ear to transmit the sound to the auditory pathways.

The complications of stapes surgery include otitis media, ear drum perforation, imbalance, taste disturbance and further hearing loss.

Conclusion

Today the patient with otosclerosis who has reasonably good inner ear function has an excellent chance of permanent restoration of hearing by modern stapes surgery.

Injustice

Whatever the human law may be, neither an individual nor a nation can ever deliberately commit the least act of injustice without having to pay the penalty for it.

— Thoreau

The Advantages and Limitations of a Hearing Aid

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A WEARABLE HEARING aid is an amplifying system designed to counteract the handicap of hearing loss by reproducing sounds at intensity levels strong enough to be useful to the patient. Clearly, a particular patient's success will depend upon three factors: (1) the adequacy with which his hearing aid reproduces sound; (2) the peculiarities of his hearing impairment, including any special problems he may have in interpreting sound; and (3) the kinds of everyday listening situations in which he must function.

Nature and Characteristics of Hearing Aids

Modern wearable hearing aids are usually of the air conduction type, consisting of five major parts: (1) a microphone that transforms sound waves into electrical patterns, (2) a transistorized amplifying circuit, (3) a battery that supplies energy, (4) an earphone that translates the amplified electrical patterns back into sounds, and (5) a hollowed earpiece that channels sounds to the ear drum.

Hearing aids do not achieve ideal sound reproduction for two reasons. First, crispness and clarity are restricted because the small size of the microphone and the earphone limit the range and the balance of the tones that are reproduced. Second, maximum output and amplification are limited not only by the instrument's small size and the problem of "squeal" but also because patients can not tolerate extreme sound levels. For these reasons the total intensity range that occurs in everyday sounds can not ordinarily be brought unmodified to the patient. When faint sounds are audible to him, the very strong sounds occurring an instant later will be distorted; while reducing the amplification to make

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strong sounds more natural will make some of the fainter sounds too weak to be perceived.

A few hearing aids are worn on the body. These are used by persons who either need particularly powerful aids or have some other special requirement, such as the young child's need to have an instrument that he can wear comfortably and safely. More commonly, hearing aids are mounted at ear level, either in the temple piece of eyeglass frames or as a separate unit. Such a mounting has three advantages: (1) the microphone participates in head movement, (2) unnatural shadowing of sound by the body is avoided, and (3) the system is less cumbersome.

Indications

No patient gains practical benefit from a hearing aid unless many of the sounds he wishes to hear are otherwise inaudible to him. Ordinarily he must expect at least some trouble in direct conversation (when loss for speech is about 45 decibels). However, some people with milder losses spend enough time in restrained group conversations, business conferences and other faint listening situations to make a hearing aid useful at least on a part time basis.

Ordinarily, the upper limit of efficient use comes when loud speech close to the ear is barely understandable (when loss for speech is 75 to 80 decibels). Persons with still greater loss even miss a good deal of amplified sound. However, their need for the limited help they do get is tremendous, and there are very few people with losses so great that they can not find properly selected hearing aids of some value.

The Young Child

The young child poses a special problem in hearing aid use. Not only must he be taught how to wear a delicate instrument, but in addition, if he has a substantial hearing defect, he will need training to counteract the slower acquisition of auditory skill which his deprivation has caused. One can not place a hearing aid on such a child and expect full elimination of his

handicap any more than one could expect him to read Persian immediately if he were given eyeglasses. Parents in particular are often unrealistic, expecting miracles as soon as the hearing aid is put on the child, instead of realizing that listening skills can only emerge slowly by combining proper training before and after acquisition of the instrument.

The Elderly Patient

Elderly persons with mild losses present a very different problem. Here the loss in hearing is primarily for higher pitched tones. This loss disrupts intelligibility by reducing the crispness of consonantal sounds. Usually there is also a general slowing of auditory interpretative capacity because of aging. When these circumstances exist a hearing aid will be of only moderate help. As an amplifier it will make very faint conversation loud enough but will not restore the dulling of clarity caused by aging. Particularly important, it will be of almost no use in the noisy and chaotic environments which older people find especially disturbing acoustically. These limitations must be recognized and accepted if the typical elderly patient is to achieve any satisfaction with a hearing aid.

The Patient with Unilateral Deafness

Until recently the patient with unilateral deafness was not encouraged to wear a hearing aid. However, an arrangement known as CROS has changed this view. CROS picks sound up at the deaf ear and feeds it into the good ear through an ear-piece that is open enough to allow sound reaching the good ear directly also to enter it unhindered.

Limitations of a Hearing Aid

Three other considerations influence the value a patient will gain in everyday life from a hearing aid.

Environment

First, since a hearing aid functions only as an amplifier, it gives the greatest help when required to reproduce sounds generated faintly in relatively quiet environments.

The patient whose life habits carry him often into such circumstances will receive much more benefit than if he were in places where competing sounds are also being amplified.

Background Noise

Second, all background noise becomes relatively more disturbing in contrast to sounds of primary importance when heard through a hearing aid. Consequently, there are noisy environments wherein a normal auditor can still function effectively but which become unintelligible bedlam for the hearing aid user. Any person with normal hearing who is not fully aware of this problem will erroneously expect hearing aid users to understand well in any environment, no matter how noisy, where he himself can. Such lack of realism discourages and disgruntles hearing aid users. Such a user must come to know accurately those circumstances in which he should expect his instrument to be of help; knowing this he can take full advantage of its benefits without expecting the impossible from it. For example, a factory worker may find an aid completely impractical on the job and of little value when things get boisterous in the neighborhood tavern, but highly useful in church, during quiet conversations at home and the like. To demand that he wear a hearing aid all the time would be to nurture frustration.

Shadowing Effects

Third, the efficiency of everyday listening is greatly influenced by the shadowing effects which the body and the head produce effects especially marked when competing sounds are present. There will then be times when these competing sounds are not shadowed, while the sounds one wishes to hear are shadowed. The masking caused at such times by background noise can be as much as 12 decibels greater than masking in the reverse situation, that is, where only competing sounds are being shadowed.

No listener using only one hearing aid can escape at least some circumstances where the balance between background noise

and primary signal is made poorer because of shadowing. The problem is reduced with an ear level instrument because the head can be turned rather quickly so that the microphone is directed toward the primary sound, but it can not be fully eliminated unless two ear level aids are worn, one on each side.

With such a binaural arrangement, one or the other of the two hearing aids will be situated so that the primary sound is not shadowed and hence is being received through one ear with the minimum competition possible at the moment. In addition, binaural reception gives an added three decibels reduction in masking of speech by noise because both ears are being stimulated. Before deciding on a binaural hearing aid, however, one must weigh the benefits thus gained against the extra cost and added inconvenience of a second instrument. A drastically new level of overall efficiency in noisy situations will not be achieved simply by donning a second hearing aid. The binaural system is a tool of major clinical importance only because the wearer no longer must cope half the time with the added disadvantage of shadowing; but it does not deliver the miracles some expect of it.

Evaluation of the Patient

Obviously, *whenever a patient can use a hearing aid to practical advantage, he should do so.* To this end, he and all who advise him must be aware of the limitations as well as the advantages. Among other things his need should be individually analyzed by an expert in hearing disorders and in the use of hearing aids. Just going out and getting "any good hearing aid" is hazardous. For one thing there are subtle engineering differences which affect efficiency of models that superficially seem similar. Secondly, the instrument (or instruments) chosen must match his requirement as to power, amplification and tonal balance.

The task of guiding the patient to successful hearing aid use begins with careful otological evaluation, since a wearable instrument is the treatment of choice only when the patient's impairment can not be amelio-

rated medically or surgically. Also, the patient's auditory capacities must be analyzed by speech audiometry, including formal testing of his efficiency while wearing hearing aids chosen to meet his needs. The results of the entire examination, interpreted in the light of the patient's living habits and the other special considerations of his case, are the basis for deciding whether a hearing aid should be advised for him. If so, plans must be made at this same time for as extensive a program of guidance and training as his case may require. Such follow-up services range from brief advisory sessions with adults who can use amplifica-

tion easily to a prolonged educational program for the young child who must develop listening skills in conjunction with his mastery of hearing aid use.

Conclusion

In conclusion, hearing aids can be great boons to hard-of-hearing patients, but serious hindrances to their use often arise. These hindrances, however, can usually be overcome by appraising realistically what the patient may expect in the way of help and by giving him thorough professional guidance in the selection and use of an instrument suited to his needs.

William Clowes (1540-1604?)

That the times produce the man has been irrefutably demonstrated throughout history — but nowhere so patently as in medical history. When a challenge arose — it was met!

One such notable challenge was the treatment of gunshot wounds, which, in England's centuries of almost unrelenting warfare, presented multifarious problems unfamiliar to surgeons prior to the discovery and use of gunpowder.

One of the men who met the challenge was William Clowes, a sixteenth-century English army surgeon, whose wide observation and practice with soldiers wounded in battle resulted in the work, "Proved Practice for Young Surgeons," used as a reference and text by students. With what ingenuity and skill Clowes solved one troublesome problem is described in Parker's "Early History of Surgery:"

"In 1573 a soldier named Giles was shown him, who had been wounded three years previously in Flanders by a bullet entering the left iliac fossa. There was still a deep sinus there, which was seriously affecting his health, and the situation of the bullet could not be determined. Clowes made futile efforts to reach it by long probes. He then enlarged the orifice, introduced sponge tents, and even caustics, but he was still unable to get a flexible probe down to find the bullet. He bethought himself that a liquid might penetrate, and injected through a long tube a solution containing alum and sublimated silver, leaving it in while the patient was kept in a suitable position. Twenty-three hours after, pain and swelling began in the right buttock near the anus, which was poulticed. Next day he cut down on the swelling, found the bullet there, and removed it. After a series of dressings and injections the wounds healed up completely."*

Clowes, however, was not the only pioneer in the field of battle injuries; there were others. One might almost say that during her military history England produced a new breed of men — her military surgeons. Instigated by a drive to meet a new and compelling challenge, these men present convincing historical substantiation for the materialistic conception of history: the theory that the times produce the man.

*Parker, G., M.A., M.D., M.R.C.S.: *The Early History of Surgery in Great Britain*. A. & C. Black, LTD., London, 1920. p. 76.

Deafness in Young Children

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MUCH HAS BEEN written in recent years concerning the deaf child, the ways to diagnose his handicap, his treatment, his rehabilitation and his prognosis. Unfortunately there is still much to be learned about children with such handicaps in spite of progress made through clinical research, pathological studies and experiments in rehabilitation in this field. In order that information can be gathered that is basic to early identification of the problem, it is necessary that the pediatrician and the general practitioner as well as the otologist be kept informed about the state of the art.

Communication

When one refers to a deaf child, one usually has the picture of a child with noticeable inability to communicate and to receive information compared to the average child of his chronological age. Communication difficulties are not necessarily due to deafness alone. There are many other factors that contribute to communicative problems in the growing child.¹

From the point of view of assembling the necessary data to make the diagnosis of hearing loss, it is of the utmost importance that all other conditions that may contribute to the child's communicative problem be identified or ruled out. Studies of a child suffering communicative difficulties should be undertaken as early as possible; therefore, the least suspicion of hearing loss or the failure to develop normal speech should alert the general practitioner, the pediatrician and the otologist to make an immediate investigation.

Causes of Difficulty

The most common causes of communicative difficulty in the young child of preschool age are: (1) hearing loss, (2) retarded

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mental development, (3) severe emotional disturbances and (4) aphasia. The child under observation, therefore, should not have his examination limited to hearing tests, but in any case where the hearing tests do not conclusively prove the handicap to be the result of hearing loss, psychological, psychiatric and neurological studies should be obtained. Many times such a battery of tests are not locally available, and it is necessary to refer children to medical centers for more definitive studies. One should always remember that children suffering communicative difficulties may also have multiple neurological handicaps.

History

Evaluation of the child should begin with a careful and complete history and be followed by certain basic examinations that can readily be made in the office of any clinician. The history which is of primary importance in these cases should include specific information in a number of areas. The areas outlined below will be of some use as a guide.

Family History

- The genetic background of the family
- The Rh factors of the parents
- Miscarriages or other obstetrical problems of the mother
- State of hearing and general mental and speech development of sisters and brothers in the family

Pregnancy

- Duration of pregnancy
- Prenatal infections, particularly those of viral origin
- Threatened miscarriages
- Unexplained fevers
- Drugs administered during pregnancy that might be considered ototoxic²

Delivery

- Onset of labor
- Duration of labor
- Position of child in uterus
- Use of forceps
- Type of anesthesia given to mother

Child's condition at birth particularly as related to cyanosis or evident trauma as a result of instrumentation. In the case of cyanosis, information should be obtained concerning aspiration, difficulty in starting respiration, duration of oxygen administered and length of time cyanosis persisted.

Development of jaundice in the newborn: degree and type of treatment

Postnatal

Health after birth and up until time of office visit

- Ear infections
- Head injuries
- Children's diseases
- Convulsive seizures
- Sleep patterns

Developmental History

Age of onset of sitting up, walking, climbing, self feeding, toilet training and speech.

A good yardstick by which to evaluate the development of a child is to remember that in normal children sitting up takes place at around six months, walking at around 12 months and speech development by the end of the second year.

Hearing

Much can be learned about hearing impairment by knowing a child's response to environmental sounds such as sudden loud noises, the sound of the doorbell and the ringing of the telephone. The child's reaction to being called from behind and from one room to the next should be ascertained and also his reaction to sounds of variable intensity such as the record player and radio. When possible it is helpful to determine *if a child understands what he is told or if speech merely acts as an alerting mechanism to get his attention.*

Speech and Language Development

Detailed information is important in this area. It has been noted in many instances that children who later develop communicative difficulties do not have a normal cry at birth or do not vocalize normally while

playing by themselves in their cribs. It has also been seen that children who do not develop speech many times fail to imitate sounds when playing with their mothers in early infancy. The language development which precedes speech really indicates the purposeful use of some sound. Language may start with the proper use of the sounds "da da" or "bye bye". It should be remembered that the sounds "da da" and "ma ma" are natural sounds made by the tongue and the lips during the growth of almost every child regardless of hearing or even brain injury. Unless these sounds are made purposefully they do not represent language or speech development. Once there is a beginning of language, speech development follows rapidly in the normally developing child. The child who does develop speech at a normal age but whose speech is difficult to understand is very likely to be a child with a partial hearing loss such as a high tone loss.

In reviewing the data assembled from a carefully taken history, it is very unusual for one to find a clear-cut picture pointing specifically and only to a hearing loss. This is because the child with a hearing loss will frequently give the impression of and a history that is compatible with mental retardation. In his frustrations he may also ape the brain-injured child, and in his inability to learn speech will simulate the aphasic. It is well to remember that the brain-injured child has a tendency to hyperactivity, destructiveness, and inability to join with the group in play situations. He has marked perseveration and an extremely short attention span.

Physical Examination

The second step in evaluating the deaf child is the examination. This starts with the ear, nose and throat and should be designed to establish the possible presence of foreign bodies in the ear, otitis media, perforations of the tympanic membrane, abnormal development of the external canals and the absence of normal landmarks on the tympanic membrane.

Hearing Tests

Following the ear, nose and throat examinations, simple hearing tests should be carried out. These can be done in the office very easily, using whispered voice sounds of ch, sh and k, calibrated rattles, sounds from a small xylophone and the sound of crushing tissue paper. All of these sounds elicit responses in the normal hearing child. A child of three months should turn toward the alerting sounds,³ all of which should be presented outside of the range of vision.

TUNING FORK

In cases of infants only a few weeks old, some information can be gained concerning their hearing or at least their reaction to sound by studying the moro response and the pinna reflex following sudden sharp sound stimuli.⁴ Much also can be learned by using a tuning fork. Such sound sources can be used equally well in infants and in young children. The tuning fork should be within the range of 500-1000 cycles so as not to transmit vibrations, and it should not be held too close to the orifice of the external canal.

It is important to remember that all hearing tests for children should be designed so as not to expose them to vibration, because their response to this can be confused with an auditory response. Coins or bunches of keys dropped on a wooden floor, or the use of large vibrating surfaces such as big pans can all give false responses.

OBJECTIVES

The primary objective of a clinical hearing test which can be done in the office is to identify some abnormality in the hearing. If such an abnormality is discovered it may be necessary to do a number of sophisticated studies which can be carried out only in a medical center in order to determine the type of hearing impairment and to rule out other conditions that simulate hearing loss.

HEARING CENTERS

Tests that are now becoming available in many hearing centers to enable a more

definitive diagnosis to be made are numerous. Those in most common use deserve a brief description.

CONDITIONING TESTS

The *peep show* in which a child is conditioned to receive an award if he signifies that he hears a test tone by some positive action such as pushing a button,⁵ and *galvanic skin resistance audiometry* where a child is conditioned by the use of a mild electric shock following the presentation of a sound stimulus.⁶ At first the skin resistance decreases following the shock; and after the child becomes conditioned, skin resistance drops following the sound stimulus in anticipation of the coming shock. Recent modifications of this test are now in use in which a single burst of tone is delivered at a fairly high intensity. No conditioning is employed, and the sound is not followed by a shock.⁷ The test can be repeated only a few times, however, before adaptation begins. In such a single burst galvanic skin resistance test thresholds cannot be obtained.

CORTICAL POTENTIALS

Evoked cortical potentials are now used to study hearing. In this test, *cortical potentials* evoked by a sound stimulus are picked up by electrodes applied to the skull.^{8,9,10,11} This test has been in use for some years. Recently using a summation computer technique, extraneous activities that are picked up by the electrodes are averaged out so that one is able to get an accurate impression of a child's auditory cortical activity. This test is now used to obtain near threshold levels of hearing. It does not, however, necessarily imply ability to understand speech. Much can also be learned by *free field* audiometry even in very young children. A sound-proof room helps to eliminate extraneous stimuli.

Final Evaluation

Combining all of these more sophisticated techniques with careful neurological, psychological and psychiatric examination, one is now able to learn a great deal about a child with a communicative disorder.

After the type of disorder and the degree of hearing loss is established, it is of the utmost importance to determine any contributing factors that may be ameliorated by surgical or medical measures. If the examination can identify the hearing loss as having a conductive type component, x-ray studies may be helpful.

Polytomograms* can demonstrate the presence or absence of ossicular chains. They can also show deformities of the round and oval windows and abnormalities of the bony cochlea.

Such surgical procedures as the construction of an external canal, the creation of a functional ossicular chain or the simple removal of the adenoids should be carried out before any decision is made on the training program.

Following any such corrections hearing tests should be repeated to establish the basic hearing loss. When this has been determined consultation should be begun with the family to develop a long-range program.

Hearing Aids

In almost all the cases where children have a hearing loss, the question arises as to the advisability of the use of a hearing aid, and the question that follows is, "At what age should a hearing aid be selected for a child?" In general, when a child suffers from a conductive hearing loss, if such a loss is bilateral, a hearing aid should be selected and it should be quite helpful. Those children suffering sensori-neural hearing loss face a much more difficult problem.

The use of a hearing aid in the child with distorted hearing will be more successful than in an aging adult, but it still leaves the child with defective speech; and if the low tones are near the normal line, the child may reject the hearing aid because of the intensity of the low tones which cannot be sufficiently suppressed when high tones are being magnified.

The child who rejects his hearing aid should be studied very carefully. The first thing, of course, that must be determined is whether the ear mold contributes to his discomfort and for this reason, he rejects

*See Test Your Word Score Page 1028.

the aid.

Alerting Mechanism

In children with severely debased hearing of a sensori-neural type, one should consider the use of an aid as an alerting mechanism rather than with the idea of restoring the threshold of hearing to a near normal level. It is extremely important with young children that they learn to associate some sort of sound with human communication even if it is only enough sound to alert them to turn their heads so that they may see the speaker.

Age to Use Hearing Aids

Hearing aids should always be used at as early an age as possible; in many instances, this seems to be between the ages of one and two years. If possible some evaluation of the type of hearing loss and the degree of loss should be established before an aid is fitted. As a rule of thumb most children who profit from the use of an aid, and this may include those extremely deaf children mentioned above, will accept the aid and show no objection to its daily use.

Children who, due to distorted hearing or extreme sensitivity to sound are made uncomfortable by loud sounds being introduced into the ear by the aid, will soon reject it. The decision to use the aid should be left, of course, until all other studies have been completed. The aid should be chosen and fitted with great care by a trained audiologist with a good clinical background.

Home Training

In general it is the consensus of opinion among teachers working with the handicapped-hearing child that where the hearing loss is not so great as to demand complete special training, it is better to keep the child in the home environment and enter him in a normal school situation, taking advantage of special preschool training that is available and the special instruction that can be obtained in a normal school program today.

In the home, especially when there are

normal brothers and sisters living with the hearing-handicapped child, conditions are better for the social and emotional development of the child.

As part of a young child's education, use should be made of home guidance courses such as the John Tracey course. The Tracey course has an added advantage in that it is of great help to the parents.

When a program is outlined, it has been the experience in this clinic that the parents need regular counseling to review with them all the advances made, all the problems still existing and the steps that must be made for further rehabilitation.

Conditions Predisposing to Hearing Aids

It should be remembered by those physicians caring for young children that a number of conditions predispose to hearing loss. Any child born following a prenatal viral infection,¹² be it rubella or any other type of viral infection, should be watched and should have his hearing thoroughly checked by the age of a year and a half to two years. Children born with erythroblastosis or with a history of a long period of cyanosis following birth should be suspect.¹³ The incidence of neurosensory hearing loss is very much higher in premature children than in full term children. Many children have hearing problems of the less severe variety due to some degree of middle-ear disease. Early recognition of such lesions is important in order to correct the lesion before it becomes irreversible.

Speech Development

It should be emphasized again and again that when a child fails to develop speech at the average normal age for speech onset and when he fails to give normal responses to sound stimuli, he should be investigated very carefully. If he is deviant in other ways as well as in his hearing responses, he should have further examinations to rule out other neurological defects. The problem facing the world today is one of early identification. It is up to the general practitioner, the pediatrician, and the otologist to have a high

index of suspicion and to insist that these children have a careful and complete evalua-

tion of their hearing at as early an age as possible.

References

1. Bordley, J. E., Hardy, W. G., and Hardy, M. P.: Pediatric Audiology. Pediatric Clinics of North America. W. B. Saunders Co., Vol. 9, No. 4, 1962.
2. Shambaugh, G. E. et al.: Dihydrostreptomycin in Deafness. JAMA 170:1657, 1959.
3. Ewing, I. R., and Ewing, A. W. G.: The Ascertainment of Deafness in Infancy and Early Childhood. J Laryng 59:309, 1944.
4. Hardy, W. G.: Examining the Young Child. Ed. Glorig, A. Handbook of Audiometry, Chap. 10, p. 207, Williams and Wilkins, Baltimore, Maryland, 1965.
5. Dix, M. R., and Hallpike, C. S.: The Peep Show: A New Technique for Pure Tone Audiometry in Young Children.
6. Bordley, J. E.: An Evaluation of the Psychogalvanic Skin Resistance Technique in Audiometry. Laryngoscope 66:1162, 1956.
7. Berlin, C.: Magnitude of Unconditioned Galvanic Responses to Tone. ASHA 6:10, 1964.
8. Marcus, R. E., Gibbs, E. L. and Gibbs, F. A.: Electroencephalography in the Diagnosis of Hearing Loss in Very Young Children. Dis Nerv Syst 10:170, 1949.
9. Derbyshire, H. J., Fraser, M. A., McDermott, M., and Bridge, A.: Audiometric Measurements by Electroencephalography. EEG Clinic, Neurophysiology 8:467, 1956.
10. Goldstein, R., Kendall, D. C., and Arick, B. E.: Electroencephalic Audiometry in Young Children. J Speech Hearing Dis 28:4, 1963.
11. Shimizu, H.: Binary Addition of Peak Times for Electroencephalic Audiometric Responses. J Speech Hearing Res 9:2, 1966.
12. Swan, C., Tostavin, A. L., Moore, B., and Barham-Black, G. H.: Congenital Defects in Infants Following Infectious Diseases During Pregnancy. Med J Aust 2:201, 1943.
13. Bordley, J. E., and Hardy, W. G.: Etiology of Deafness in Young Children. Acta Otolaryng 40:72, 1951.

Heart Diagnostics in Ancient Egypt

The Scribe of the ancient Egyptian Papyrus dealing with medicine was evidently cognizant of the physiological-emotional reactions of the human heart. He appears to have been sure of himself; neither incertitude nor inhibition is detectable in his naive and rather touching exposition:

When anger arises in his heart, behold it is a seething-up of the parts of the Intestine and the Liver. His Ear is on the alert, his vessels fall after their rising heat has dissolved everything.

When the Heart is sad, behold it is the moroseness of the Heart, or the vessels of the Heart are closed up in so far as they are not recognizable under thy hand. They grow full of Air and Water.

When the Heart feels an aversion, behold it is the Bitterness of the Heart because of Inflammation in the Anus. Thou findest it big and something forms itself in his Abdomen as in his Eye.

Praise from a Scholar

Antiquity rightly both believed and proclaimed that no reward worthy enough can be paid to a skilled and trustworthy doctor . . . The theologian makes men repent of their sins, but it is owing to the doctor that there is anyone to repent. It is vain to be a physician of souls if the soul for whom the antidote was prepared has already fled . . . We owe gratitude to those who drive off the enemy who flies at our throats; are we not more indebted to the doctor who daily fights for our safety against the mortal enemies of life? — Erasmus (1466-1536)

Principles in Rhinoplasty

IRVING B. GOLDMAN, M.D.*
New York, New York

SUCCESSFUL RHINOPLASTY is based on anthropology, physiognomy, genetics, diagnosis, physiology, psychological therapy, anticipated healing properties of the tissues, and art anatomy with appropriate esthetic appreciation. The deformity must be studied, the nose properly analyzed, and the general facial impression noted. All the above mentioned components must be integrated before surgery. The surgeon must deliberate upon what he wishes to do, but what is more important he must consider what potentials are involved in obtaining a satisfactory result.

Indications for Rhinoplasty

As one becomes experienced in rhinoplasty, it becomes apparent that trends change from the viewpoint of esthetic results as well as surgical techniques.

Esthetic

The geographical habitat of the individual has a direct bearing on the overall indications for corrective rhinoplasty, as well as the desired cosmetic result. The primary motives for those seeking a rhinoplasty are unchanged; the esthetic, functional, and especially the psychic still prevail. Function is important, but those seeking a rhinoplasty will frequently use this medium as a subterfuge because they do not like the appearance of the nose. It becomes obvious that nasal dysfunction, so common in many people, is merely the starting point for demanding a cosmetic operation. Obviously, a badly disfigured nose is often accompanied by a severely deviated septum; but the majority of those seeking a rhinoplasty have minimal septal abnormalities.

Functional

Some rhinoplastic surgeons assert that

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they carry out septal resection or reconstruction in 75-80% of their patients. Others do it routinely to prevent constriction of the airway by the infractured lateral nasal walls. One has only to experience a nasal collapse after performing these combined procedures to recognize and respect the stabilizing function of the septum. Excessive sacrifice of the septum and subsequent loss of support of the dorsum, in addition to the frailty of the nasal structures because of loss of stability of the underlying septum, should induce the surgeon to ponder before he weakens that formidable structure. The septum operation that I have sponsored for many years, namely minimal removal and replacement, still prevails today. Many nasal complications are caused by the loss of the supporting role of the septum. In a combined rhinoplasty and septal reconstruction, partial or total collapse of the nasal pyramid may result from loss of support of the scaffolding septum after osteotomy of the nasal walls and mesial shifting of the nasal processes.

Surgical Management

Proper prophylactic management of the obstructing septum and specific technical steps must be undertaken to prevent dropping of the residual nasal bones and lateral nasal processes as well as the upper lateral cartilages, which can produce a saddle of either the osseous or cartilaginous vaults or both. Roentgenograms taken of such complications of total collapse show these vaults to have fallen almost into the floor of the nasal chambers.

The Anesthesia

Apprehension of needle injections for local anesthesia is widespread. Patients are advised that the operation is painless but that the solution must be injected for anesthetic as well as hemostatic purposes and for aiding undermining of the nasal integument. Some surgeons use inhalations of trichloroethylene to dull the consciousness before the anesthetic is injected. I have been using a Panjet syringe initially, preparing the regions for deep penetration when the local anesthetic is injected. As a result, the com-

mon complaints about painful needle injections have almost completely disappeared. The Panjet compresses a 1/10-cc. volume of anesthetic solution and, when the release button is depressed, emits the compressed liquid in the form of a fine jet spray which penetrates the surface to a controlled depth of 2 to 6 mm. No needle is used and the controlled region of perfect subtopical anesthesia is painlessly achieved. Painless wheals are raised through which the needles are inserted. Some anxious patients insist on intravenous demerol for the rhinoplasty. I agree to the intravenous demerol or similar drugs but, in collaboration with the anesthetist, the intravenous anesthesia is kept at a minimum because of the preliminary local anesthesia with the Panjet syringe. The complications from intravenous demerol and the long periods of unconsciousness following the operation have been eliminated by the diminished intravenous dosage.

Mesial Osteotomy

After hump removal the mesial osteotomy, usually by a chisel, is carried out in order to facilitate symmetrical mesial shifting of the nasal pyramid to the midline after the lateral osteotomy. By this pressure impact on the lateral nasal wall the nasofrontal articulation is severed. Many of the pioneers in rhinoplasty avoided the mesial osteotomy; others objected that a low fracture would result, producing a wide radix. This may be true, but the lateral walls of the radix are readily amenable to instrumentation, producing the desired normal width of the bridge of the nose. The mesial osteotomy causes a loose or frequently comminuted fracture after lateral osteotomy and mesial shifting of the nasal bones and processes. Avoidance of the mesial osteotomy results in a more stable osseous pyramid after infracture. Protruding bones on either side of the root of the nose can be easily smoothed by the fine rasp or under direct vision by the bone clipper. Obviously, if a nose is very broad because of wide nasal bones and radix, mesial osteotomy is required to remove wedges of bone for closer approximation. Under these circumstances the integument

and procerus muscle help camouflage smaller bony irregularities which may be difficult to smooth or level because of their extreme mobility.

To help avoid the mesial osteotomy I have found it expedient to shave the most superior ventral thick block at the radix. Frequently after the hump has been removed, a slightly elevated bony dorsum can be seen and felt cephalically. To reduce with safety this shallow but thick bony projection to the proper profile line I have devised a "plane" chisel. The upper dull prong rests on the bones as a protection against removing too much bone. The cutting chisel is attached beneath and slightly posteriorly. Depending on how much the "plane" chisel is angulated, one may remove bone dust or 1 mm. of the solid bone at the nasal root. This bony removal also helps to narrow the nose after mesial shifting of the frontal nasal processes which fracture high or very close to the nasofrontal articulation. To lower a high nasofrontal angle the "plane" chisel can be reinserted and more bone removed safely (Figure 1).

Modeling the Tip

As we discuss modeling of the tip it becomes apparent that the mesial crura are the salient factors in tip projection and in tip rounding or drooping. The parts of the nasal tip to be modeled include the columella which is in line with the height of the nostrils, the lobule, the structure above the

nostrils reaching the apex of the tip, the nasolabial angle, and the slope of the nostrils. These definitive structures can be modeled only if the entire lower lateral cartilage extending into the lobule is completely freed from the overlying skin. Naturally this requires more time, skill, and patience. The tip which I have described fulfills all requirements for precise modeling. The low columellar sutures will bring about the desirable nasolabial angle. The freed, bisected and sutured mesial crura will help model the lobule, give the required projection, influence the slope of the nostrils and produce the desired "double break" which takes place between the straight or slightly curved columella and the angulated lobule. A tip is produced that not only looks good on the operating table but retains its appearance permanently.

The Age Factor

In young patients the lower lateral cartilages are very frail, thin and underdeveloped. After surgery they may heal with a fibrous tissue curtain resulting from contact between the extremely thin and loose lower lateral cartilage and the septum. I have been consulted by patients who were operated on at age 12 and revised at age 13, in whom an artificial cul-de-sac completely occluded the nasal vestibules. I believe that the opportune age for a rhinoplasty in young patients depends essentially on the degree of development of the lower lateral cartilages. Mani-

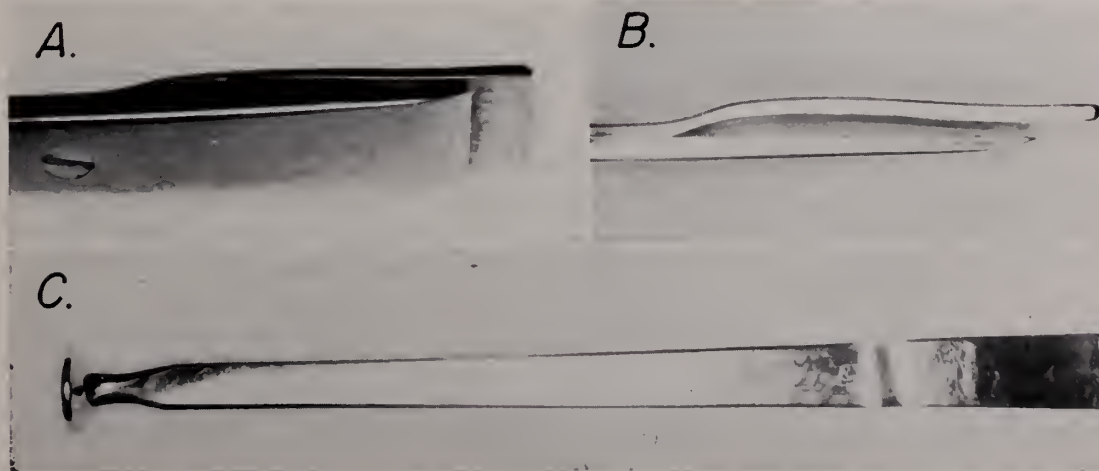


Fig. 1 (A) — Side view of "plane" chisel from above; (B) Lateral view showing dull protecting blade superior to cutting chisel below; (C) "Plane" chisel from above. Photographs are enlarged.

festation of firmness of the cartilage on palpation serves as a criterion for carrying out a suitable rhinoplasty. The cartilaginous rigidity begins to manifest itself after 15 or 16 years of age. At an earlier age removal of the cartilage not only may cause nasal obstruction or alar collapse, but can also produce a poorly corrected tip because its immature skeletal composition lacks molding adaptability especially of the mesial crura which serve as the fulcrum for the new tip. Healing of the overlying skin is unpredictable.

Conclusions

The principles of rhinoplasty have been modified by the changing esthetic objectives

of the patient as well as of the surgeon, and by advancements in the technical approaches. Much can be done in order to obtain a natural, normal functioning, non-surgical appearing nose. Where the perspective is unattainable the rhinoplastic surgeon must abstain from performing esthetic surgery. The overly ambitious who have attempted impossible procedures have learned to use better judgment in the screening of patients for corrective nasal surgery. In cosmetic rhinoplasty the surgeon should learn to distinguish between the favorable and unfavorable variety of patients in order to obtain the most satisfactory results. Mediocrity is no longer acceptable.

The Frontier Doctor III*

At the end of a long and wearisome ride, the doctor set broken limbs, bound up wounds and injuries, delivered babies, fought smallpox, pneumonia, and diphtheria. His cures were blunt. He slit the throat of a child choking with diphtheria and opened the windpipe. He kept the aperture from closing with fishhooks. A frontier doctor's cures were vigorous too. Seizing a patient sick with fever, the doctor opened a vein and drew blood until unconsciousness was near. This lowered the heart action. The patient broke into perspiration. His fever and delirium vanished. The doctor next administered tartar as an emetic and followed it with a calomel purge. Finally he "locked the bowels," as the expression went, with opium. When the doctor paid a return visit, the patient usually declared himself "well, if a little weak," most likely to prevent additional treatment. The doctor was ingenuous too. If a man broke his leg, he reduced the fracture and tied rough-hewn shingles on each side of the break. To keep the leg pulled straight, he constructed a traction apparatus with a rope and a flatiron or a few horseshoes.**

*See Minnesota Med 50:643, 1967.

**Richard Dunlop, M.D.: Doctors of the American Frontier.

A Physician's Voice from Ancient India

By the sense of *hearing* we can, for instance, determine whether the contents of an abscess are frothy and gaseous, for the emptying of such is attended with noise; by the sense of *feeling* we may know whether the skin is hot or cold, rough or smooth, thick or thin; by the sense of *sight* we can determine corpulence or emaciation, vital power, energy, and change of color; by the sense of *taste* we can assure ourselves concerning the state of the urine in diabetes and other diseases of the urinary tract; and by the sense of *smell* we can recognize the peculiar perspiration of many diseases which has an important bearing on their identification.

— Susruta (6th Century B.C.)

Diseases of the External Ear

Current
Status

BEN H. SENTURIA, M.D.*
St. Louis, Missouri

DISEASES OF the external ear occur in 5% to 10% of patients seen in a general ear, nose and throat office practice. Preventing diseases of the external ear is difficult; however, some factors contributing to the development of some of these diseases are known.

Classification

The author, in collaboration with M. D. Marcus in 1952, published a classification of diseases of the external ear which incorporates dermatologic as well as otolaryngic concepts and principles. This increasingly accepted classification, modified to incorporate some of the more recent developments, is as follows:

Diseases of Unknown Etiology

- A. Malfunction of Skin Glands
 - 1. Seborrheic Dermatitis
 - 2. Asteatosis (Dry Ear)
 - 3. Hyperceruminosis
- B. Infantile Eczema
 - 1. Infantile Intertrigo
 - 2. Infantile Dermatitis
- C. Membranous External Otitis
- D. Chronic Idiopathic Myringitis
- E. Lupus Erythematosus, Psoriasis, etc.

Diseases Due to Infections

- A. Bacteria
 - 1. Gram-positive
 - a. Furunculosis
 - b. Impetigo
 - c. Pyoderma
 - d. Ecthyma
 - e. Cellulitis
 - f. Erysipelas
 - 2. Gram-negative
 - a. Diffuse External Otitis
 - b. Bullous External Otitis
 - c. Granular External Otitis
 - d. Perichondritis
 - 3. Acid-fast

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B. Fungi and Yeasts (Otomycosis)

1. Saprophytic
2. Pathogenic

C. Virus

1. Bullous Myringitis
2. Herpes Simplex
3. Herpes Zoster
4. Molluscum Contagiosum
5. Variola and Varicella

D. Protozoa

E. Parasites (Animal)

Neurogenic Eruptions

A. Simple Pruritis

B. Neurodermatitis

1. Localized
2. Disseminated

C. Neurogenic Excoriations

D. Artifact Dermatitis

Allergic Dermatoses

A. Contact Type Dermatitis (Dermatitis Venenata)

B. Atopic Dermatitis

C. Drug Eruptions

D. Infectious Eczematoid Dermatitis

E. Physical Allergy

Traumatic Lesions

A. Contusions and Lacerations

B. Surgical Incisions

C. Hemorrhages

1. Hematomas
2. Vesicles and Bullae

D. Trauma

1. Burns
2. Frostbite
3. Radiation Injury
4. Chemical Injury

*Senile Changes**Vitamin Dyscrasias**Endocrine Dyscrasias***Etiology**

Convincing evidence exists from human and animal investigation, that gram-negative bacilli are more common in the diffuse external otitis type of infection while gram-positive organisms are found in the eczemas, furuncles, etc. Of course, fungi continue to be the most important agent in the otomycotic lesions. Temperature and humidity are now thought to play an important role in the incidence of diffuse external otitis; but less understood are the roles of skin lipids, excessive sweating, stress, and anatomical configuration in the causation of these diseases. Likewise, PH of the ear secretions and allergic factors are poorly understood etiologically, but little evidence exists to confirm these as important factors in the causation of non-allergic external otitis.

Treatment

Unfortunately, there is a tendency to give the same "shot-gun" prescription for all forms of external otitis. A common mistake is that of giving penicillin injections and ear drops in an oily vehicle for typical diffuse external otitis infections due to an overgrowth with gram-negative bacilli. Serious, resistant infections with irreversible sequelae may result from this error. Oily drops are also contraindicated in acute diffuse external otitis; drying and soothing agents are a better treatment.

Eyes are compacted powers; they are an index of vision; they see and refer us to greater seeing. Nor has the stomach a less noble office. It digests food; that is, in its own particular method, it deals with the nourishment offered by the universe. It is the physical formula of that health which destroys certain elements — the bacteria which harmfully approach us. By it we learn to consume; by it therefore to be, in turn, consumed. So even with those poor despised things, the buttocks. There is no seated figure, no image of any seated figure, which does not rely on them for its strength and balance. They are at the bottom of the sober dignity of judges; the grace of a throned woman; the hierarchical session of the Pope himself reposes on them. — Charles Williams

Plastic Surgery of the External Ear

RICHARD T. FARRIOR, M.D.*
Tampa, Florida

THE GENERAL PHYSICIAN has become increasingly aware of the need for correcting deformities of the external ear and increasingly informed regarding some of the surgical procedures available, which he might recommend to his patient. Deformities of the external ear, for our purposes in this presentation, are divided into two general groups: first those involving the simple protruding ear, and second, those requiring more extensive reconstructive surgery with or without the loss of tissue.

The modern otolaryngologist is intimately familiar with the anatomy and all diseases of the external ear and is trained in the reconstructive procedures of the auricle and external canal.

The Protruding Ear

Medicine generally has come to accept the value of esthetic procedures in the improvement of the overall well-being of the patient, particularly in these times when a premium is placed on appearance and the stresses of the modern age make it desirable to reduce the deleterious psychological effects of a deformity when this is at all possible.

The deformity of the protruding ear, more than others, fosters a reaction of mirth from other people, instead of inciting sympathy as with other deformities, and the child is constantly reminded of his defect. The adjustment an adult may have to uncorrected protruding ears is influenced by his individual personality, but even most adults in honesty to themselves do not like their protruding ears. Most are very keenly aware that the ears they are endowed with may interfere with their personal relationships, both economic and social. The deleterious psychic effects make these deformities of clinical significance.

Emphasis is placed on the normal contour

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of the ear as seen from the side. There are numerous procedures for correcting the protruding ear, but many have shortcomings in terms of recreating exact contour. The modern otolaryngologic plastic surgeon should be precise in his technique and attempt to mimic nature as accurately as possible.

Operative Procedure

The operation for correction of protruding ears may be performed under local or general anesthesia and produces minimal discomfort or morbidity. For the psychological reasons discussed, it is beneficial to have the operation performed by six years of age; however, many operations are performed in adults. Most patients are in the hospital only overnight. A splinting ear dressing is worn for from five to seven days.

The Antihelix

Luckett, in 1910, first emphasized that the antihelix was the primary area involved in the abnormally protruding ear. Many operative procedures have been developed, designed at either breaking or weakening the cartilage spring and creating a normal angulation of the ear. As seen from the side many of the procedures create abnormal angulation or visible incisional lines which are distracting. The late Doctor Oscar Becker contributed as much as any one man to the modern concepts of analysis of the deformity and attention to details.

The technique I developed is aimed at creating normal contour with predictable results, and it incorporates techniques which take into account all the many variable anatomic factors which contribute to protruding ears.

Technique

The technique includes both breaking the cartilage spring by carefully placed incisions about the inferior portion of the antihelix and weakening the spring by the removal of longitudinal cartilage wedges which do not create abnormal angulations on the anterior surface. The latter is particularly important about the superior crus. These re-

moved longitudinal cartilage wedges do not extend through the thickness of the cartilage.

The technique as mentioned takes in all contributing factors in the production of the protruding ear even though all may not be involved in a particular case. By following this technique the young surgeon is less apt to create disappointing results.

Suturing Technique

In recent years the simple suturing technique has been repopularized and, has given satisfactory results particularly in young children with delicate cartilage, provided the normal anatomy is critically analyzed in regard to placing of the sutures. In the simple ear in young people without too much cartilage resilience and not too deep a conchal cartilage, the simple technique may work.

Problems

The simple suturing technique does not take into account all factors contributing to the particular deformity. Among these we would have to consider:

A pillar effect of the inferior crus is sometimes encountered.

Success depends upon the degree of the existing convexity of the antihelix, the degree of the existing concavity of the scaphoid fossa, and the development of the antihelix. With the simple suturing technique there is a backward tilting and flattening posterior to the antihelix which may occur in a flat ear where there is no scaphoid fossa and minimal helical rim. The suturing technique does nothing to create the scaphoid fossa.

Nothing in the simple suturing technique accounts for the deep cupped conchal cavity where it is essential to remove some cartilage to reduce the cup. It is interesting that since the revival of the simple suturing technique many surgeons are now adding modifications and are facing up to more complicated procedures. This results from improper analysis in some cases of the contrib-



The author emphasizes normal contour as seen from the side. Note the gradual convexity of the superior crus blending with the fossae on either side, the continuous blending of the crura with the antihelix proper, the acutely convex antihelix proper gradually widening superiorly, and the definite scaphoid fossa. Normal projection with the preservation of the auriculomastoid angle is obtained.

uting abnormalities.

In summary, our technique is perhaps more complicated for some ears; however, it takes into account all factors and all possible pitfalls.

Reconstructive Procedures

Apart from the simple protruding ear, deformities of the external ear may be divided generally into those with and without the loss of tissue. Only soft tissue may be involved or there may be a loss of cartilage framework.

The nature of the thin, relatively adherent skin on the anterior surface of the ear, and the contoured and delicate, yet definitely supporting cartilage present major problems in reconstruction. Without loss of tissue, surgery usually involves excision of excesses or rearrangement of the existing skin or cartilage. It may be necessary to elevate the surface of the skin, refashion the existing cartilage, and then redrape the skin in the new contour.

The most common deformities are those with defects and loss of tissue. The absence of soft tissue or cartilage may be the result of congenital anomalies, trauma with avulsion, or surgical defects usually excisional for carcinoma.

Although blood supply in general is good, reconstruction of the surface layers and the intervening and supporting cartilage keeps the surgeon in a critical state of balance between viability and esthetics. The latter usually suffers to some degree.

Congenital Anomalies

These deformities may range from simple preauricular appendages or fistulas to total absence or severe microtia* with stenosis or atresia of the canal. The surgeon must present an honest and frank appraisal to the parents or to the older patient. The limitations of the final results in total reconstruction, the number of stages, and the psychological aspects of the surgery itself should be outlined and the patient allowed to make the decision to proceed.

If one is honest in his presentation, he frankly finds himself with few total reconstructions to do. These are done with fair success, serve the purpose of eliminating the need for a prosthesis, and provide an ear constructed from the patient's own tissue. Recent attempts in a significant series, utilizing the silicone rubber pre-made framework, have in the majority of cases proved disappointing and in one way or another have presented or required eventual complete removal and replacement with autogenous cartilage. The repair should be closely correlated with the indications and techniques for middle ear surgery.

Traumatic Surgery

Traumatic surgery requires careful closure in layers of lacerations through the cartilage. I see no objection to approximating the cartilage with sutures through the thickness of the cartilage, although this continues to be frowned upon by some. Retrieved, avulsed portions of the auricle should be thoroughly cleaned and delicately sutured in position to produce accurate approximation without impairment of the blood supply. Major loss requires the same consideration as for excisional defects for cancer.

Carcinoma

Carcinoma of the external ear requires vigorous excisions, staying one jump and one natural tissue barrier ahead of the lesion. If cancer of the external ear extends to the mastoid bone, the prognosis is grave. Where the skin is mobile, the underlying cartilage and bone should be excised. With bone or periosteal involvement en bloc, radical resection is essential. Small marginal defects may be treated by x-ray or electrodissection, but these defects are also readily excised and repaired, thus avoiding x-ray over the auricular cartilage.

Repair of Large Defects

Repair of larger defects in most instances requires the use of the postauricular sulcus skin or skin over the mastoid process. A

*See Test Your Word Score Page 1028.

pocket may be fashioned to receive salvaged auricular cartilage or an implant for reconstruction of the framework. This pocket is utilized to transfer skin to the anterior surface of the ear. For smaller defects I have had some success with homogenous preserved cartilage, polyethylene or silicone implants; but I have stayed with autogenous costal cartilage for major reconstructions.

The postauricular skin may be used in a variety of ways as advancement and rotation grafts. If tubed pedicle grafts become necessary, these can more often be fashioned in the periauricular area or from the immediately adjacent cervical skin.

Ear Remnants

All possible remnants of the ear should be saved, either to aid in reconstruction or for the attachment or support of a prosthesis. Some reconstructive procedures may be necessary simply to aid in the wearing of a prosthesis. Where some portion of the ear remains, reconstruction has much to offer. As mentioned, total reconstruction has definite limitations.

The Canal

Surgery of the canal requires judgment regarding the margin of excision and some knowledge of temporal bone surgery, both to prevent stenosis and to preserve maximum hearing. Reconstruction beyond the bony canal should not be attempted unless the surgeon or a member of his team is prepared to do the full range of modern middle ear surgery, tympanoplasty, and indicated stapes or fenestration surgery. Facial nerve surgery must be anticipated but is not for discussion here.

Conclusions

Protruding Ears

Emphasis is placed on creating normal contour of the ear as seen in the lateral view, as well as correcting the protrusion. The otoplastic surgeon should attempt to duplicate natural appearance as nearly as possible. The technique developed is directed towards these goals. Postoperatively, the gradual convexity of the superior crus, without visible incision lines or angulations, is desired. The antihelix proper is subtly prominent and there is a definite groove between the antihelix and helix.

The general physician and the pediatrician are encouraged to be aware of this readily correctible deformity and recommend the procedure, especially where it seems important in the particular individual for his overall well being and outlook.

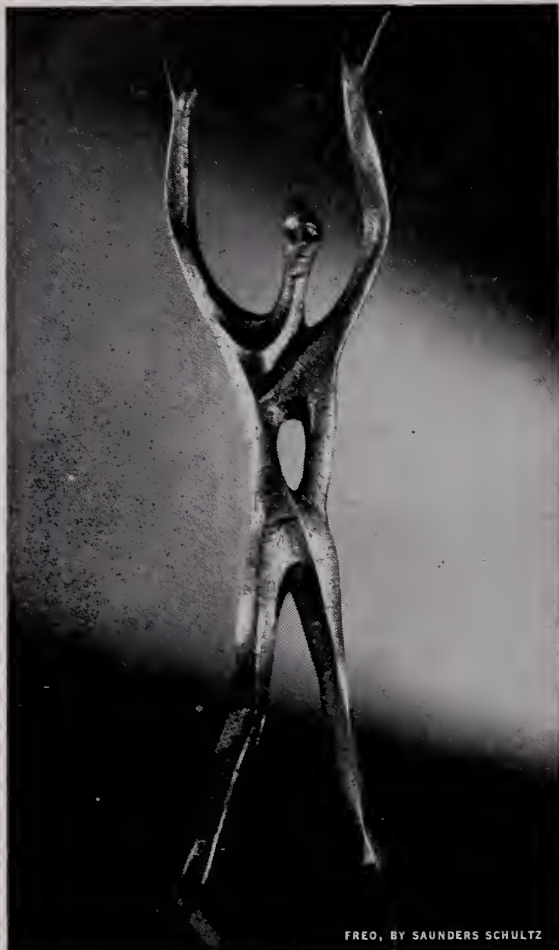
Reconstructive Procedures

Reconstruction of the external ear requires the incorporation of all plastic surgery principles, particularly in the use of both implants and grafts. Combined skin grafts utilizing a variety of both free grafts and grafts bearing their own blood supply must be in the armamentarium. Wherever possible, autogenous implant material is advocated.

In carcinoma, radical excision is essential. For carcinoma of the ear, remove underlying cartilage and bone. If the lesion escapes to the middle ear or mastoid bone, the prognosis is most guarded. If there is any question regarding the margin about the lesion, no principles of cancer surgery should be violated and reconstructive procedures should be disregarded. In most instances, however, some form of primary reconstruction is possible and desirable.

O Thou, who know'st the wants of human kind,
Vouchsafe me health of body, health of mind;
A soul prepared to meet the frowns of fate
And look undaunted on a future state;
That reckons death a blessing, yet can bear
Existence nobly, with its weight and care.

— Juvenal (60-140)



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Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently.

Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonamides, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage. Make regular blood counts. Discontinue the drug and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The most common are nausea, edema and drug rash. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, or a generalized allergic reaction may occur and require withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

Dosage in Osteoarthritis: The initial daily dosage in adults is 300-600 mg. in divided daily doses. When improvement occurs, dosage should be decreased to the minimum effective level; this should not exceed 400 mg. daily, and is often achieved with only 100-200 mg. daily.

For complete details, please refer to full prescribing information. 6562-VI(B)R

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Chronic Nasal Dysfunction

FRANCIS L. LEDERER, M.D.*
Chicago, Illinois

A SLANG EXPRESSION, "Plain as the nose on one's face," dates back to the year 1660. This still holds over three centuries later as the story of the nose in health and in disease begins to unfold. The nose is the gateway to life and death (Holden) and while in many languages, including Hebraic, the words for "breath" and "soul" are practically identical, a more modern version would be to say that the nose is indeed State and Madison Streets of the respiratory tract. From an anthropomorphologic point of view the nose-form frequently identifies ethnic origin, tribal custom, as well as the happy hunting ground of physiognomists. Modern man's involvement in high speed driving, the manly art of self-defense, and other body contact sports frequently produce the battered nose syndrome, altering both appearance and function.

As originally blueprinted by the Master Architect, the contour and the composition of the framework of the nasal pyramid, as well as the design, content and type of lining of the cavity, were calculated to meet the needs of man. The external supporting structure serves to maintain and protect the airway to insure the primary function of respiration in warming, moistening and cleansing of air, as well as the secondary functions of olfaction, phonation (resonating chamber), gustation,** temperature adjustment, absorption as a therapeutic pathway, drainage and bacteriostasis. It may come as a surprise to some that the sense of smell is comparatively unimportant clinically and is rudimentary in man, yet the sensitivity is startling. The many environments man elects to live in have brought into play the importance of the nose as a humidifier, 1000 cc. of water being evaporated every twenty-four hours. This varies inversely with the humidity outside: when hot and humid, there is but little evaporation

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**See Test Your Word Score Page 1023.

from the nasal mucosa; when dry, there is considerable.

Normal nasal function depends upon six basic requirements:

1. Large surface area, including turbinates.
2. Moist surface (mucus sheath).
3. Movement and replenishment of mucus by cilia and glands.
4. Heat supply, in which the cavernous spaces are neither contracted nor engorged.
5. Proper biochemical composition of secretion, about a pH of 6.5.
6. Normal pathway for aeration.

When there is an absence of normal function as a basis for dysfunction, it could be represented either by hyper- or hypofunction as compared in the following tabulation which gives some indication of the wide variety of intrinsic and extrinsic factors which must be considered.

Nasal Function		
Normal	Hyper-	Hypo-
Anthropomorphic	Irritative	Abnormality
Respiration	a) Temporary	a) Developmental
Humidification	b) Prolonged	b) Acquired
Olfaction	Allergic	Medication
Ventilation	Medication	Febrile states
Drainage	Foods	Constitutional or
Filtration	Carbohydrates	systemic disorders
Ciliary action	Starches	Endocrine
Phonation	Climatic	imbalance
Gustation	Environmental	Psychogenic
Bacteriostasis	Infectious	
Barometer of emotions	Endocrine imbalance	
	Psychogenic	

No approach to a proper diagnosis of cause and effect will ever be superseded by the thoroughness inherent in a good history, a competently carried out physical examination, including anterior and posterior rhinoscopy, supplemented by laboratory aids when indicated by the findings. In accordance with an old aphorism, "Seeing is believing but feeling is the naked truth," probing and palpation with applicator and canula are important to correct diagnosis as well as treatment. To the experienced clinician the color, texture and contour of mucous membrane constitute valuable signs. The presence of secretion, whether watery, mucoid, suppurative, hemorrhagic or crusted, may

likewise figure prominently in arriving at a diagnosis of nasal dysfunction.

The abundant vascular supply of the nose and the relative accessibility of vessels, including *epistaxis digitorum* and *epistaxis feminis*, identify nosebleed as a most frequent dysfunction, represented as a primary or reflecting an underlying pathophysiologic phenomenon. Specific disease entities, including cardiovascular abnormalities, febrile states, exanthem, collagen aberrations, hematopoietic disturbances and hereditary multiple angiomas are occasionally associated with pulmonary arteriovenous phenomena.

Not only is the richness of the nerve supply of the nose the site of origin and the recipient of numerous reflex arcs but it also responds to fear, exaltation (the barometer of our emotions), as well as many modern vasoconstrictor and decongestant agents introduced into the nose and the anti-hypertensive *Rauwolfia* drugs popularly prescribed for oral administration. A boggy, wet, pale white mucosa may relentlessly block the nose until the pharmacologic relationship is discovered. It is of interest to note that the bouts of migrainous neuralgia are accompanied by a unilateral red eye, the production of tears and nasal stuffiness. The innumerable other causes of nasal dysfunction, particularly those producing nasal obstruction, are summarized as follows:

I Extranasal

A. Congenital Defects

1. Narrow bone bridge
2. Atresia of nares
3. Thick columella
4. Collapsed alae
5. Depressed tip
6. Dilated alae

B. Acquired Defects

1. Depressed fracture
2. Displaced cartilages
3. Atresia of nares
4. Neoplasms

II Intranasal

A. Congenital

1. Nasal septum
2. Lateral walls
3. Posterior choanal

B. Acquired

1. Nasal septum
 - a) Hematoma
 - b) Abscess
 - c) Deviations

2. Nasal cavity
 - a) Infection
 1. Acute
 2. Chronic
 3. Specific
 - b) Foreign bodies
 - c) Rhinoliths
 - d) Adhesions and synechia
 3. Lateral Nasal Wall
 - a) Simple rhinitis
 - b) Hypertrophic
 - c) Atrophic
 - d) Vasomotor
 - e) Hyperplastic
 - f) Purulent
 - g) Neoplastic
 - h) Specific
 4. Floor of nose
 - a) Cysts
 1. Nasoalveolar
 2. Nasolabial
- III Nasopharynx
- A. Adenoids
 - B. Neoplasms
 1. Local origin
 - a) Benign
 - b) Malignant
 - c) Specific
 2. By extension
 - a) Choanal polyp
 - b) Nasopharyngeal fibroma
 - c) Malignant tumor

At this point of the discussion it becomes apparent that chronic nasal dysfunction may be many things in many people. The

need to bear them all in mind is obvious but not necessarily to oversimplify the problem or to focus attention on the nose as the prime diagnostic target. While the blotchy mucosal pallor of vasomotor rhinitis, as more or less a subclinical type of allergy, constitutes the most frequently encountered cause of nasal blockage, offending allergens in themselves may be a considerable source of dysfunction. On a similar basis, the sneeze, the secretion, the anosmia and the obstruction may be associated with hyperplastic mucosal changes of varying degrees. The presence of polyps may reflect similar degenerative changes in any or all of the nasal accessory sinuses, at times as one part of the interesting triad of situs inversus and bronchiectasis or another disease combated with difficulty, viz., cystic fibrosis. When polyps are unilateral, neoplasia, such as inverted papilloma, or even malignant change must be ruled out by the careful histological study of all tissue removed. To end this discussion of a unilateral nasal blockage on a less sombre note, it may be that a foreign body or even a rhinolith may produce sizeable granulomas to confound the experts.

Medical Eponyms from England

In the first half of the nineteenth century, English physicians gave their names to various diseased conditions: Joseph Hodgson described dilatation of the aortic arch (Hodgson's disease, 1815); James Parkinson, paralysis agitans or shaking palsy (Parkinson's disease, 1817); Richard Bright, nephritis, or disease of the kidneys usually associated with dropsy and albumin in the urine (Bright's disease, 1827); Charles Bell, peripheral paralysis of the facial nerve (Bell's palsy, 1829); Thomas Hodgkin, malignant lymphoma, or involvement of the lymph nodes with enlargement of the spleen (Hodgkin's disease, 1832); Thomas Addison, pernicious anemia (Addison's anemia, 1849), and disease of suprarenal capsules (Addison's disease, 1849) — an early landmark in the coming science of the ductless glands.*

*Victor Robinson: *The Story of Medicine*.

Peach Leaves

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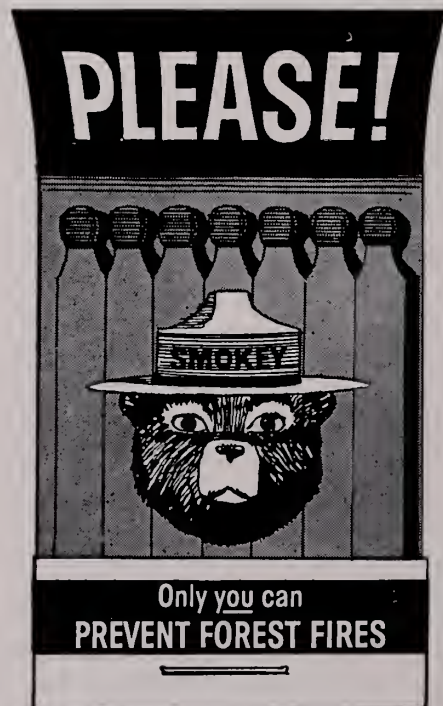
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|| Epistaxis*

WILLIAM H. SAUNDERS, M.D.**
Columbus, Ohio

TRAUMA SHOULD be considered as the factor common to most cases of nosebleed. Anteriorly, the injury may be quite obvious, such as the trauma inflicted by picking the nose, or it may be more occult as when caused by excessive drying of the mucosa. Blowing of the nose may tear crusts from the mucosa and thus open blood vessels. Frequently the margins of a septal perforation crust and bleed.

Posteriorly, this sort of external trauma is not likely to occur. Instead, epistaxis frequently results from splitting of a sclerotic vessel caused by infection of the mucosa or hypertension. Often there is no obvious cause.

Common Errors and Misconceptions

Before describing the correct methods of diagnosing and treating nosebleed, there are several common errors or misconceptions that deserve emphasis.

Bilateral Bleeding

Rarely do patients bleed from both sides of the nose simultaneously. If blood comes from both sides, it is because it passes behind the nasal septum from one side to the other. Patients with blood dyscrasias or with severe facial fractures may bleed from both sides; others should not be expected to do so.

Arterial Ligation

Ligation of the external carotid artery for epistaxis is rarely indicated. It must be remembered that not all of the nasal blood supply is derived from the external carotid artery; bleeding may come from branches of the internal carotid artery. In these cases, the ethmoidal vessels may be ligated. Again, such a procedure is rarely required. Nevertheless, many carotid ligations have

*See Test Your Word Score Page 1028.

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been done to control epistaxis. *In most instances, more efficient packing would have served better.*

Pharmaceutic Preparations — Their Misuse

When nasal packing is improperly placed and the patient continues to bleed, doctors sometimes prescribe a drug supposed to control bleeding. Except in rare instances in which the patient is bleeding because of an actual deficiency of vitamin C or vitamin K, such preparations have no value.

Use of drug therapy in treatment of nosebleeds is often harmful because it causes the physician to rely upon a medical treatment for a surgical condition. The doctor administers drug therapy instead of removing poorly placed packing and repacking accurately at the bleeding site. Many drugs have been recommended and used in the treatment of ordinary nosebleed. Instances in which use of these drugs seemed effective should be reevaluated. It must be remembered that time is a factor in nosebleeds. Given enough time (whether or not these products are being used) most nosebleeds will stop spontaneously.

The best parenteral therapy for the patient with ordinary epistaxis is a narcotic like morphine or a sedative like seconal. The best pharmaceutic agents for topical use are adrenalin and chemical cauterants.

Death from Nosebleed

I have never seen a patient die because of nosebleed although I have treated at least three patients each of whom during their lifetime bled enough to require over 2000 blood transfusions. Patients become deathly pale and they faint, but they do not die. (Some authorities have reported death from coronary insufficiency secondary to severe nosebleed, but such instances must be extremely unusual.) When a patient bleeds enough to go into shock, his blood pressure falls and his bleeding is reduced to a trickle or it stops. Thus there tends to be a check on the amount of blood a patient can lose from epistaxis at any one time.

Conditions Not Causing Nosebleed

It is almost as important to emphasize conditions that are not the cause of nosebleeds, except rarely, as to emphasize those that are. Physicians who are not adept at intranasal packing and cautery often attribute nosebleeds to a disturbance in the blood clotting mechanism. A physician may pack the nose of a patient but not place the packing accurately; the bleeding then continues. Instead of replacing the packing the doctor mistakenly assigns the cause of bleeding to a supposed (but rarely present) hematologic disturbance. Alterations in the vitamin K or vitamin C blood levels, or changes in the prothrombin time, bleeding time, or clotting time, are not commonly the causes of epistaxis. When epistaxis is due to systemic causes such as scurvy, leukemia, or a change in the blood prothrombin level, the patient bleeds from various mucous membranes and into the skin and viscera. Why should a patient with a generalized hematologic disturbance bleed only from the nasal mucosa? The answer is that he doesn't or does so only very rarely, and then soon bleeds from another site. Nosebleed in a patient who is not bleeding from any other part of the body is almost always the result of local trauma.

Treatment

Most physicians at one time or another have had to treat a patient with nosebleed. Otolaryngologists may have this as a daily or weekly experience. There are different approaches, but each is arrived at by first identifying the exact bleeding site and, second, by stopping the bleeding by using cautery or by placing packing accurately.

The nose usually bleeds from one of three sites: (1) anteriorly at Kiesselbach's plexus on the septum, (2) from far posteriorly under the inferior turbinate, (3) from posteriorly and high in the nose (from the anterior ethmoidal artery). It is very important that the physician determine from which area his patient is bleeding because the treatment of anterior bleeding, which is simple, differs entirely from the treatment



Figure 1(a)



Figure 1(b)



Figure 1(d)



Figure 1(c)



Figure 1(e)

Fig. 1 — Treatment of nosebleeds from the anterior part of the nose. (a) First step — sucking clots and blood from the nose. Note gowns on both the patient and the doctor. (b) Second step — application of epinephrine to a cotton ball. (c) Third step—compression of the cotton for several minutes against the bleeding septum. (d) Fourth step — cautery of the bleeding vessel with a silver nitrate stick. (e) Same as (d) but using an electric cautery instead of silver nitrate.*

*From DeWeese, David H., and Saunders, William H.: Textbook of Otolaryngology, Ed. 2, St. Louis, 1964, The C. V. Mosby Co.

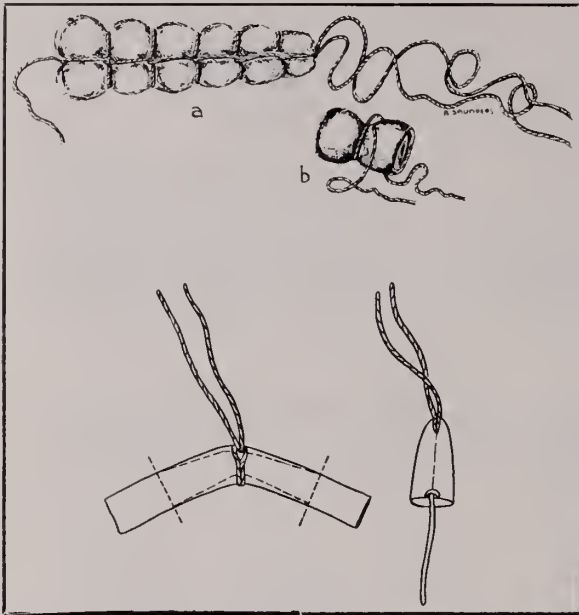


Fig. 2 — a, Three strings are needed. b, Packs can be made from roller bandage or gauze, but care must be taken that they are not too large or they will not only obstruct both choanae but also block the eustachian tube. This pack should also have a third string to dangle in the nasopharynx to make removal easier. c, Construction of a postnasal pack from a vaginal tampon.*

of posterior nosebleed. The treatment of the two different posterior nosebleeds also differs.

Anterior Nosebleed

All that is needed to control this bleeding is a bright light to help identify the bleeding spot, suction to clear the nose of blood and clots, and some form of cautery. Aqueous adrenalin, 1-1000, applied to cotton and inserted into the bleeding side (with pressure on the ala) will help control the bleeding until the doctor can perform cautery.

Figure 1 demonstrates the exact steps in identifying and controlling an anterior nosebleed. Note that the patient and doctor are gowned (a "must" in dealing with epistaxis); note also the use of chemical or electrical cautery. In the case of chemical cautery (usually a silver nitrate stick) local topical anesthesia is sufficient — cocaine 5 percent or pontocaine 2 percent is effective. For electrical cautery, injection of the mucous membrane with 1 percent xylocaine is advisable.

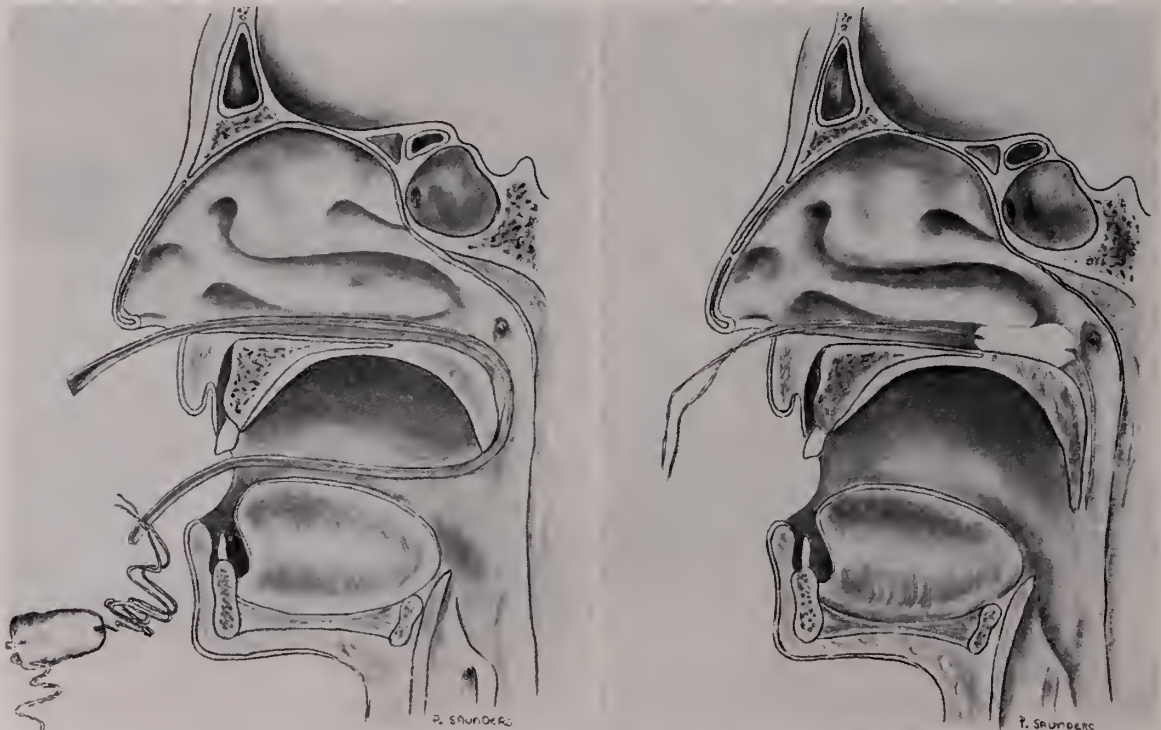


Fig. 3 — Postnasal packing. a, (left) First step. b, (right) Second step. Anterior packing with 1/2-inch petrolatum gauze is then placed. In addition to petrolatum it is well to lubricate all packing with an antibiotic ointment to prevent infection and odor.*

*From DeWeese, David H., and Saunders, William H.: *Textbook of Otolaryngology*, Ed. 2, St. Louis, 1964, The C. V. Mosby Co.

No packing is required after cautery of an anterior bleeding site.

The anterior ethmoidal artery bleeds from high and posteriorly in the nose and it can bleed briskly. To identify the exact bleeding site one needs a brilliant light (preferably a head mirror reflecting light from a 150-watt clear bulb) and a sucker to clear blood. By advancing the sucker tip further and further into the nose one comes to a spot where suddenly no blood appears. This indicates that the blood is going directly into the tip of the sucker.

With the exact spot of bleeding identified, a compressed cotton ball about as big as a bean, impregnated with vaseline or terramycin ointment, is pressed hard into the space between the septum and the middle turbinate (the superior meatus). This small pack should stop the bleeding, but to hold it securely additional packing of the superior meatus with one-fourth inch gauze stripping, again well greased, is advisable. Four or five days later, if bleeding has been checked, the packs are removed.

Posterior Nosebleed

Often occurring in older persons, these nosebleeds may come from the very back of the nose and usually from under the inferior turbinate. They are difficult for both patient and doctor. First, the bleeding from here is profuse and second, it is very difficult to work adroitly in the posterior nose where visualization may be difficult even in a patient without a nosebleed. Spot cautery is not possible in most instances and one must resort to the postnasal pack to control bleeding.

Figure 2 shows different types of postnasal packs. The essentials are that the pack not be too large — it need fit only one posterior choana and should not obstruct the eustachian tube; that the pack have strings attached anteriorly and posteriorly and be well greased.

Greasing with terramycin is recommended because packs greased in this way have no odor when removed and lack of odor implies lack of infection.

The postnasal pack must be seated *very*

firmly by strong traction on the two stout anterior strings (Figure 3). Then the anterior part of the nose is carefully and firmly packed with gauze stripping which again is greased with antibiotic ointment. Packing is removed in two or three days and replaced if there is recurrent bleeding. Patients requiring a postnasal pack should be in the hospital.

Blood Transfusions

If a patient is in shock due to blood loss, immediate transfusion may be required. Often, however, paleness and faintness are due not to blood loss but to the discomfort associated with placement of a postnasal pack.

There is a false sense of security that comes from checking the hemoglobin imme-

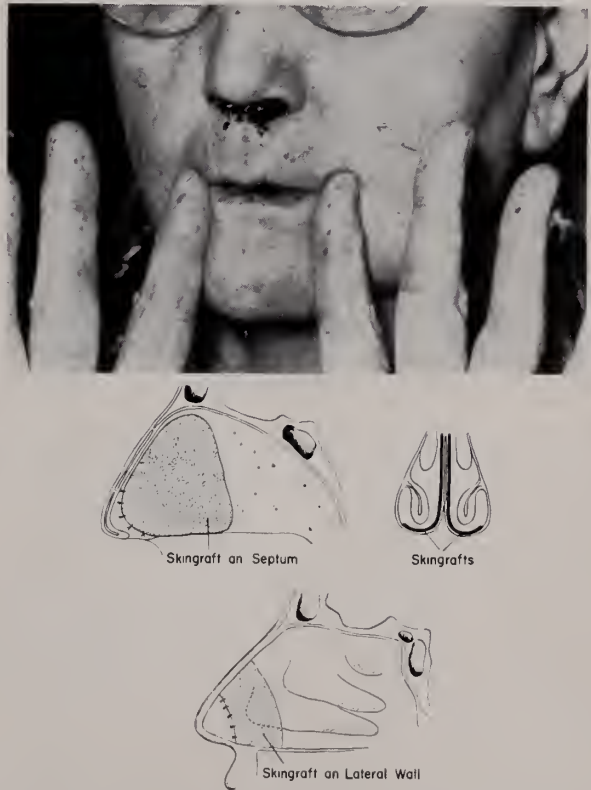


Fig. 4 — a (top) Severe nasal crusting like this is common in patients with hereditary hemorrhagic telangiectasia. Note also telangiectasia on lips, fingertips, and face — all common sites. b, (bottom) Septal dermoplasty operation. The skin grafts can be considered posterior extensions of the normal vestibular skin.*

*From Saunders, W. H.: Hereditary Hemorrhagic Telangiectasia: Its Familial Patterns, Clinical Characteristics, and Surgical Treatment. Arch Otolaryng 76:245, 1962.

diately after a severe nosebleed. The hemoglobin concentration which has occurred gives relatively normal values for hemoglobin, whereas the next day, after hemodilution has occurred, the patient's hemoglobin determination indicates severe anemia.

Hereditary Hemorrhagic Telangiectasia and Nosebleeds

The severe, repeated, life-long nosebleeds that mark hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease) are known to most otolaryngologists. Nosebleeds which usually begin about puberty become worse as the patient grows older. A hemoglobin determination of four grams is not infrequent. Some patients with this disorder also bleed from the gastrointestinal tract and, in fact, hemorrhage has been reported from virtually every body orifice and into most organs.

This special type of nosebleed can now be controlled effectively by a surgical procedure called septal dermoplasty (Figure 4). In this operation the principle is to replace the

fragile epithelium in the anterior one-third of the nose by a split-thickness graft of skin from the thigh. The skin graft, being tough, resists trauma and prevents bleeding. Results in over 100 patients demonstrate that the procedure is effective. Some patients never bleed again, while others, who do bleed occasionally, do so much less severely and less often.

Another treatment for patients with bleeding from hereditary hemorrhagic telangiectasia is the use of ethinyl estradiol. This drug, given in a dosage of 0.25 mgm. daily, is said to convert the respiratory epithelium into a squamous epithelium. Thus it attempts to do medically what septal dermoplasty does surgically. Side effects of loss of libido and hypertrophy of the male breast may be serious. The medication must be used lifelong.

Patients who suffer seriously from nosebleeds caused by hereditary hemorrhagic telangiectasia should first have a septal dermoplasty. For those who need further help because of persistent bleeding a trial on estradiol is in order.

Hernia on the Frontier

Range doctors dealt frequently with hernias. Oregon doctor, J. R. Jonson, was called on a case of strangulated hernia. The sick man writhed in agony, and his abdominal muscles were so tense the doctor could not do a thing. He had no drugs with him and was as helpless as the crowd of sympathetic bystanders who had gathered around. One man squirted a stream of tobacco juice toward a spittoon.

"Bite off another chew," said the doctor.

When the man did, Dr. Jonson took the tobacco and inserted it into the patient's rectum. The nicotine quickly brought on a cold sweat and nausea. Muscles relaxed, and the doctor was able to reduce the hernia.

Richard Dunlop, M.D.: *Doctors of the American Frontier*

Ladder of Hermes

The Ladder of Hermes was a preparation contrived by Gilbert of England in the thirteenth century. It consisted of 60 simples, compounded by arithmetic progression into one all-purpose prescription: One ounce each of four simples plus two ounces each of four more simples plus three ounces each of four more, etc., until all 60 were incorporated into the final product.

This 15-step Ladder of Hermes was reputed to possess phenomenal potency in curing more than just 15 diseases!

Chronic Sinus and Broncho- Pulmonary Diseases

The Relationship

F. W. DAVISON, M.D.*
Danville, Pennsylvania

NUMEROUS MEDICAL articles of 20 to 30 years ago discussed the relationship between chronic sinus diseases and various types of chronic bronchopulmonary disease. Some pointed out that the chronic sinus disease was primary and the bronchopulmonary disease secondary.

Other authors thought that the pulmonary disease was primary and the sinus disease secondary. To substantiate this claim they cited the fact that cough and expectoration are not socially acceptable, so that in order to get rid of secretion the person with bronchiectasis would cough tracheobronchial exudate into the nasopharynx and then blow it into a handkerchief.

Investigations

Most authors, however, felt that the sinus disease was primary. To substantiate this claim animal experiments were done in which India ink was injected into the cavity of the maxillary sinus and was demonstrated in the lymphatics and also in the pulmonary tissues. This experiment was thought to establish that the mode of extension of the infection was by way of the lymphatics. Subsequent investigators showed rather more conclusively that in the first experiments large amounts of India ink were used, some of which overflowed into the nose and nasopharynx and was aspirated into the tracheobronchial tree.

They further demonstrated that the lymphatic drainage of the sinuses is into the retropharyngeal lymph nodes. Other investigators placed iodized oil in the nose while patients were asleep and later demonstrated its presence in the tracheobronchial tree by roentgen examination. Therefore this possible mode of extension of infection is apparently well established.

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Aspiration of infectious material can undeniably initiate a bronchopulmonary infection. That this sequence of events is not inevitable is demonstrated by the large number of people who have chronic suppurative sinus infection of many years' duration but do not have any bronchopulmonary disease or symptoms.

Upper and Lower Respiratory Tracts

Something that needs re-emphasis is the fact that the upper and lower respiratory tracts are one physiologic unit and that mucosal misbehavior in both areas often has a systemic cause predisposing to disease in *both* areas.

Some of the systemic or constitutional diseases which predispose to infection in both upper and lower respiratory tracts are allergy, the antibody deficiency syndromes, cystic fibrosis, endocrine disturbances, especially poor adrenocortical function, malnutrition and other chronic debilitating diseases.

Rhinosinusitis and Bronchiectasis

One of the more frequently noted associations is the coexistence of chronic hyperplastic rhinosinusitis and bronchiectasis. In 1944 I wrote a paper entitled "Does Chronic Sinusitis Cause Bronchiectasis?" My conclusions were as follows: (1) chronic sinusitis and bronchiectasis frequently coexist, but one does not cause the other; (2) all patients in this series who had both bronchiectasis and sinusitis were of the hypersensitive type; (3) the allergic or hypersensitive state was an etiologic factor in 80 per cent of this series of 50 cases of bronchiectasis; (4) seventy-two per cent of the 50 patients developed bronchiectasis during the first decade of life; (5) seventy-four per cent traced the onset of their chronic cough to an acute bronchopulmonary infection; (6) mucosal edema was probably the chief factor responsible for the atelectasis which led to the development of bronchiectasis; (7) our results in the prevention and treatment of bronchiectasis will be improved when we know more about hypersensitivity and how to control it.

Administration of antibiotics to kill the germs and of corticosteroids to reduce the mucosal edema have greatly improved the results of treatment of these patients.

Thirty years ago in an effort to determine the inter-relationship between sinus disease and bronchopulmonary disease I analyzed the charts of 100 patients whose chief symptoms were chronic cough, chronic nasal discharge or bronchial asthma. Only those cases were included in this study in which sinusitis was possibly a factor.

In addition to the usual history and physical examination all patients had roentgen study of the sinuses and lungs. Bronchoscopic examination and bronchograms were made when necessary to clarify the diagnosis.

This study resulted in the following classification.

Classification of Chronic Non-Tuberculous Respiratory Disease

In Non-Allergic Individuals. (45 cases)

1. Suppurative sinusitis of nasal origin. (13 cases)
2. Suppurative sinusitis of dental origin. (9 cases)
3. Suppurative sinusitis. Suppurative bronchitis. (2 cases)
4. Suppurative sinusitis. Bronchiectasis. (14 cases)
5. No sinusitis. Bronchiectasis. (7 cases)

In Allergic Individuals. (55 cases)

1. Suppurative sinusitis. No bronchitis. Asthmatic symptoms. (9 cases)
2. Suppurative sinusitis. Suppurative bronchitis. Asthmatic symptoms. (17 cases)
3. Suppurative sinusitis. No bronchitis. No asthmatic symptoms. (7 cases)
4. Hyperplastic sinusitis. No bronchitis. Asthmatic symptoms. (8 cases)
5. No sinusitis. Suppurative bronchitis. Asthmatic symptoms. (7 cases)
6. No sinusitis. Nonsuppurative bronchitis. Asthmatic cough. (7 cases)

It is evident from this survey that different combinations of disease states occur. I think this classification is still valid. The

present day availability of antibiotics and corticosteroids has tremendously improved our therapeutic results. Prompt administration of these two agents will rapidly control the *acute* infections that formerly resulted in chronic sinusitis or bronchiectasis or both.

Treatment

Sinus disease should be treated on its own merits medically and/or surgically according to the judgement of the otolaryngologists. Many of the patients with bronchopulmonary symptoms were benefited by sinus surgery, but the results were not predictable. To achieve maximum benefit for the patient it is necessary to consider systemic defects such as allergy, metabolic disorders and immunologic deficiencies which sometimes contribute to perpetuation of the disease in both areas.

When considering the relationship of sinus infection to bronchial asthma I had the concept that if we treated the sinus infection by antibiotics or by surgery we were eliminating the bacterial protein, the antigen which could trigger an allergic reaction in a sensitized bronchial mucosa.

Nasopulmonary Reflex

Bray describes a mechanism which gives another possible explanation for the improvement we sometimes see in asthmatics following sinus surgery. He quotes Adam in picturing the asthmagenic area of the nose which begins with the lower margin of the middle turbinate and includes all of the upper air passage extending from this margin to the cribriform plate, both the lateral and septal surfaces of the nose being included. Sensory impressions gathered from this area pass through the sensory portion of the trigeminal and down the descending root of the trigeminal nerve to end at about the cells of the nucleus ambiguus, which represents the motor root of the vagus and glossopharyngeal nerves. In brief, these connections explain how stimuli arising in the ethmoid region of the nose may lead to bronchospasm through this nasopulmonary reflex.

One way to demonstrate this reflex is by

mechanically stimulating the middle turbinate with a cotton-tipped probe. Usually this stimulus results in a cough rather than a sneeze.

Cystic Fibrosis

Another type of disorder which affects both the upper and lower respiratory tracts is cystic fibrosis, also known as mucoviscidosis, which affects the upper respiratory tract almost as frequently as the lower respiratory tract. Before the correct diagnosis was established, a great many of these cases had been treated for asthma, bronchiectasis, or severe allergy of the nose and sinuses.

Cystic fibrosis is recognized today as one of the more common chronic diseases of childhood and adolescence and represents the most serious lung problem among American children. It also accounts for the majority of pediatric patients with chronic nontuberculous pulmonary disease. This disease entity deserves wider recognition and study by otolaryngologists. A good source of information is the "Guide of Diagnosis and Management of Cystic Fibrosis," published by the National Cystic Fibrosis Research Foundation.

Sinusitis and Asthma

Chronic hyperplastic rhinosinusitis and bronchial asthma frequently coexist. In 1963 I reported the study of the case histories of 50 patients who had a *severe* degree of chronic hyperplastic rhinosinusitis treated surgically, who had been observed by me over a period of at least five years. After carefully reviewing the case histories of these 50 patients it was found that asthma was totally relieved or greatly benefited in 16 of the 21 asthmatic patients. However, it must be pointed out that these patients also received antibiotics and corticosteroids.

The treatment methods which stood out as being really useful were: (1) antibiotics in bactericidal doses; (2) surgery to remove tissues which had suffered irreversible damage and also to provide ventilation and drainage; (3) management of coexisting food or inhalant sensitivity; (4) oral administration of 5 to 10 mgm. of Prednisone

for a month following operation.

Conclusions

My conclusions were as follows: (1) hyperplastic sinusitis is a manifestation of bacterial allergy (delayed hypersensitivity); (2) complete surgical removal of diseased tissue is necessary in advanced cases; (3) a temporary or permanent subclinical adrenocortical insufficiency is a conditioning factor leading to the development of this type of disease; (4) patients with this disease have an inherited or acquired endocrine defect predisposing them to recurrence; (5) small maintenance doses of corticosteroids can prevent recurrence.

Antibody-Deficiency Syndromes

In the last five years the antibody-deficiency syndromes have come to be recognized as factors predisposing to frequently recurrent infections in both the upper and lower respiratory tracts. Children with both the congenital or acquired forms of hypogammaglobulinemia are especially susceptible to purulent sinusitis and pneumonia.

If untreated, many of these children acquire chronic progressive bronchiectasis and ultimately die of their pulmonary complications if they survive the innumerable acute infections. These children with low gamma-globulin levels are especially susceptible to

the pyogenic organisms, principally the ubiquitous staphylococci, pneumococci, streptococci and hemophilus influenzae.

The acute infections can usually be readily controlled with antimicrobial chemotherapy; but if treatment is delayed or neglected the bronchopneumonia, sometimes diagnosed as "whooping cough," causes sufficient tissue damage to result in bronchiectasis. This is especially likely to happen in children who also have the atopic constitution. It is easy enough to understand how this oversight can occur, because when the child is at home and the diagnosis of a contagious disease such as whooping cough is made, it is thought best not to take the patient to a hospital or other facility where a chest x-ray might be obtained.

In going over the case histories of a series of 50 patients who had bronchiectasis it was found that 30 attributed the onset of their chronic cough to pneumonia and three to whooping cough.

Summary

When chronic suppurative disease is present in both the upper and the lower respiratory tracts the physician should look for a systemic predisposing defect such as the atopic constitution, the antibody deficiency syndrome, cystic fibrosis or a metabolic or endocrine insufficiency.

Hippocrates on the Post-Hoc-Ergo-Propter-Hoc Fallacy

In convalescence from disease, as also in protracted diseases, many disturbances arise, some spontaneously, some also from things the patient happens to take. Now, suppose that on the day when such perturbations arise, any innovation chances to have been made, such as a bath or a walk having been taken, or something unusual eaten; I know that, even if these were all perfectly proper, yet the bulk of physicians, just like the laity, would nevertheless ascribe the cause to one of these things, being ignorant of the true cause, and obscuring what was probably the most useful thing that could have happened. This should not be: one ought to know the effects of a bath or toil engaged in, at the wrong time; the same mischief will never arise from both of them nor from repletion, nor from such and such a food.

It is the manner of hypochondriacs to change often their physician... for a physician who does not admit the reality of the disease cannot be supposed to take much pains to cure it. —William Cullen

Maxilloethmoidal Polyposis

A Dystrophy of the Retropharyngeal Lymphatic System

THE ETIOLOGY of this dystrophy of the intranasal and intrasinal structures is so confused that the writer will not attempt to add to the confusion except to state that many but not all of the patients suffering from this condition apparently have an inherent and inheritable allergic diathesis which may appear clinically with a variety of presenting symptoms which often include sequentially: hay fever, nasal and/or sinal polyposis and bronchial asthma.

Boies¹ stressed the importance of "prolonged allergic conditions and marked edema within the mucous membrane causing a prolapse of the tissue with the resulting characteristic grape-like masses producing annoying symptoms of nasal obstruction, pressure, and excess secretion." Thompson² observed that "nasal polypi chiefly occur between the ages of 20 and 30 and are said to be more common in men than in women. They are rarely found in the young. In 10,000 patients observed in ten years, only six cases were met with in children, the youngest being six and one-half years." Lacoarret³ observed that a malignant growth or meningocele may be concealed by or mistaken for a nasal polypus.

Increased Lymph Flow

During episodes of severe reaction to infectious or allergic stimuli, the physiopathologic basis for the formation of most of the polypi occurring in the maxilloethmoidal area is related to the proclivity of, and necessity for, the sinal mucosa and turbinal tissue to increase their volume and approximate the capacity of or completely obliterate the air-containing cavities of the nose and paranasal sinuses. The necessity for this functional pathology stems from the need for an

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increase in production of capillary filtrate, tissue fluid and volume of lymph flow during pathologic states so that a constantly changing pericellular environment may be maintained for the cells of these tissues.¹¹

Lymph Node Obstruction

A variation of this etiologic process is the lymphedema and/or polypoid protrusions of the mucosa formed due to blocking of the lymph flow through the retropharyngeal lymph nodes during malignancy and specific diseases such as glanders and diphtheria, the pathogens or toxins of which produce swelling and blocking of the lymph nodes. This latter type of intrasinal edema and intranasal turgescence is often preceded and accompanied by effusion into the tympanums which usually begins unilaterally and is frequently the chief complaint of the patient.^{12,16,23}

Defects

Premature involution and atrophy²¹ of the lymph nodes and/or congenital localized gross tortuosity of the lymph vessels have been described by Yoffey and Courtice²⁰ as the cause of congenital lymphedema and elephantiasis of the leg. A similar process may be the cause of unilateral polyposis which, if occurring in the young, may be intractable and not curable by insertion of balloons into the maxillary sinuses. However, in certain patients much can be accomplished by very frequent polypectomy.

During mild reactions such as those following temperature changes and/or transient irritation by bacteria and/or allergens, the nasal and sinal tissues may promote physiologically adequate lymph flow solely by swelling against their own inherent tissue pressure. However, during severe reactions to infection and/or allergic stimuli, these tissues may have to swell sufficiently to obliterate their air-containing cavities with an incompressible medium so that the pulsations of the dilated arterioles and arteriovenous anastomoses may be transmitted to the lymph vessels and increase lymph flow through the lymph nodes, thereby fa-

cilitating the processing and removal of the increase in products of cell metabolism, toxins, bacteria, particulate matter, viruses and proteins not used as food by cells of the part.¹¹

Pathophysiology

The sinal cavities are rudimentary at birth. During infancy and childhood the nasal and potential sinal cavities can be filled readily by swelling of their turbinal tissue and mucosa, and lymph in the absence of lymphatic obstruction is propelled easily through the comparatively numerous lymph channels and retropharyngeal lymph nodes where antibodies are formed as the body begins to develop its acquired immunity. As the sinuses develop air-containing cavities normally they are lined by mucosa which is "seldom more than .02 mm. in thickness"⁵ and is a nonabsorbing membrane because it has no interstitial spaces.⁴ When normal, the maxillary sinal mucosa probably possesses the least tissue pressure of any tissue of the body. This is evidenced by its tendency to become edematous during primary hypoproteinemia* due to albuminuria, as is seen so often in nephritis and/or malnutrition during childhood. This type of edematous sinal mucosa may be erroneously diagnosed by x-ray as sinusitis of bacterial origin.

The low tissue pressure of this mucosa aids in understanding the process of "taking cold" or cold allergy which is, quoting from Dorland,¹³ "a condition manifested by local and systemic reactions, mediated by histamine, which is released from mast cells and basophils as a result of exposure to cold." This concept of circulating histamine would portend that the sinal mucosa due to its low tissue pressure would be the first tissue to become edematous during "taking cold." The excess tissue fluid derived from this process, depending upon the nature and amount of its protein content, would stimulate a compensatory turgescence of the turbinates as they promote the flow of lymph from the sinuses.¹¹

During purulent infection, as this very thin mucosa becomes edematous and approximates the capacity of the sinus, it with the

*See Test Your Word Score Page 1028.

aid of its cilia forces the sinal secretion through the ostium. Following completion of this mechanical process there remains in the very edematous sinal mucosa a large amount of highly proteinized tissue fluid. If the physiology of the lymphatic system of this region is like that of most of the other parts of the body, the protein in this fluid will be returned to the veins after it has been processed while passing through at least one lymph node. Certain small protein molecules such as ptomaines, venoms and toxins may be absorbed directly by the veins without previous processing by the lymph nodes. The possibility of the nasal and sinal mucosa acting as an organ of excretion of its highly proteinized tissue fluid will be discussed in another sequence in this paper.

During allergic reactions, as histamine is released in the nasal and sinal mucosa, an increase in permeability of the capillaries occurs and there may be rapid effusion of filtrate which contains comparatively little protein. This type of effusion is exemplified by the quick swelling and rapid disappearance of the edema of hives and angioneurotic edema and is evidence confirming the low protein content of effusion due to purely allergic reactions. This rapid absorption is noted particularly when the time of absorption is compared with the prolonged swelling of the tissues following subcutaneous hemorrhage.

The foregoing description of some of the physiologic principles of the lymphatic system should be considered as being applicable to the general principles of the physiology of the lymphatics in most of the areas of the body. These principles are applicable to the nose and paranasal sinuses, but their adaption to these areas, particularly as they relate to the processes of capillary filtration of protein and lymph flow and immunity, is modified by developmental, anatomical and aging characteristics which set this area apart from the other areas of the body.

One of the most essential and important physiologic characteristics of the body is the ability of the blood capillaries to selectively filter into and remove from each part of the body only those components of the blood

which promote the special physiology and functional pathology of the part. Could the mucosa of the nose and paranasal sinuses with its specialized physiology also have a selective excretion function? This function of excretion could have a dystrophy which would cause retention within the interstitial spaces of the mucosa of tissue fluid containing proteins derived from the blood which, if they exist in a state of conglutination,¹⁵ might not be excretable through the mucosa. In proportion to their effective osmotic pressure these nonexcretable proteins hold the water component of the tissue fluid in the mucosa. Following recurrent episodes of increased capillary filtration due to infection and/or liberation of histamine during allergic reactions, the interstitial spaces of the mucosa become widely dilated and alternating areas of fibrosis, and dilated tissue spaces appear first in the sinal mucosa and later along the lymph channels in the middle meatus. Presence of this type of lymphedema for a protracted period of time may produce this type of dispersed areas of fibrosis in other areas of the nasal mucosa. During episodes of stress, as the tissue pressure rises in this type of mucosa, polypoid protrusions of the mucosa are formed from the areas of dilated tissue spaces.

Recognition of the sinal and/or the nasal mucosa as an organ of excretion is enhanced by the observation that normally the inside of the nose is practically sterile.² Thompson emphasizes the secretory functions of the nose when he states, "It has been estimated that in 24 hours over a liter of water is supplied by the nose and there are no arrangements in the mouth, pharynx or windpipe for secretion of any such quantity. The importance of these bacterial functions is realized by remembering that at least 10,000 litres of air pass through the nose in 24 hours and that at the lowest estimate 1,500 organisms are inhaled into the nose every hour." Also he emphasizes the necessity of "respecting the erectile tissue of the nose, as the ciliated epithelium, when once destroyed, is never renewed. It is better to be a partial mouth breather than to have free nasal passages with these protective mem-

branes seriously damaged."

Remington¹⁴ et al. recently published a significant contribution to knowledge of the defense mechanism of the nose which also is in accord with the writer's theory that the nasal and sinusal mucosa have as one of their necessary and vital physiologic and functionally pathologic proclivities, the excretion of protein, the quantities and types of which are related to the etiology and characteristics of the capillary filtrate and tissue fluid and the magnitude of the tissue pressure of the area occupied by the tissue fluid. Quoting the Summary of Remington et al.,¹⁴ "Serum proteins and antibody activities were found in nasal secretions of normal and allergic individuals. The serum proteins in highest concentration were gamma 1A globulins and albumin; gamma 2 globulins were present in all specimens, but in lower concentrations. Antibody activity to tetanus and diphtheria toxoids and streptococcal M. protein was found in nasal secretions of normal volunteers whose sera showed high titers to the same antigens. Reagenic antibody activity was demonstrated in the nasal secretion of allergic individuals, but not in those of non-allergic persons. The possible role of nasal secretions in host immunity and nasal allergy is discussed." This article by Remington et al. is worthy of attention by those interested in allergy and immunology, and their findings are in accord with the opinion of Drinker and Yoffey¹ concerning the lymph nodes as sites of antibody formation. The nodes may even be instrumental in the production of a general immunity. McMaster and Kidd⁸ (1937) suggested that "the immunity conferred by clinical Jennerian vaccination may be largely of lymph node origin."

Retropharyngeal Nodes

The lymph nodes as sites of antibody formation apparently is one of the most important considerations of the etiology, progressive development and ultimate morbidity of maxilloethmoidal polyposis. The intranasal and intrasinus structures, the adenoid, nasopharynx, eustachian tube and middle ear develop from the embryonic first

branchial pouch. The lymph from all of these structures flows into the pre-eustachian tubal lymphatic plexuses¹⁶ and then into the retropharyngeal lymph nodes. There is free communication between these plexuses across the nasopharyngeal surface of the soft palate. This free communication allows lymph from physiologic or pathologic processes on either side to flow into the retropharyngeal nodes of one or both sides. This anatomic development is responsible for the occurrence of otitis media with effusion in the contralateral ear due to unilateral infection and/or malignancy in the nose, paranasal sinuses and nasopharynx.^{11,12,13}

The retropharyngeal lymph nodes are present at birth but exist as islands of lymphocytes along the lymph pathways. As the necessity for production of antibodies occurs during childhood these islands develop into two chains of nodes.¹⁹ The relative frequency of occurrence during childhood of retropharyngeal abscess due to suppuration arising in a retropharyngeal node and the relative absence of this condition in the adult is some evidence of atrophy of these lymph nodes. The writer investigated the presence of these nodes in relation to otitis media with effusion. Under the supervision of Dr. Donald Duncan, head of the Department of Anatomy in the University of Texas Medical Branch, and his associates, sixty cadavers of adults were dissected by medical students with particular relation to the presence and location of the retropharyngeal lymph nodes. In one cadaver one node was found immediately under the eustachian tube; in four cadavers there were no lymph nodes discernible by gross inspection. This apparent atrophy of these nodes was reported in 1942 as one factor in the etiology of effusion in the middle ear due to lymphatic blockage of a semiatrophic lymphatic system.¹² The physiologic atrophy of these lymph nodes apparently occurs as a defense mechanism which reduces the probability of abscess occurring in the very vital regions of the base of the skull.²¹

The table of the relative amounts of protein present in the plasma and in polypi in patients having maxillary ethmoidal polypo-

sis reveals that the differential in the osmotic pressure between the fluid in the polypi and the plasma is of a magnitude which precludes fluid in the polypi being absorbed readily by the blood. This type of polyposis nasi, like the solitary choanal polypus, usually has its beginning as a generalized or localized edema of the nasal mucosa long before polypi appear in the nasal cavities. As the edema of the mucosa increases, there is a loss of the inherent contractility and tissue pressure of the mucosa, as stagnant tissue fluid accumulates and dilates the tissue spaces.

Tissue pressure is related to the following variables taken in part from Drinker and Yoffey^{4,11,20}:

1. According to its magnitude tissue pressure resists capillary filtration and promotes capillary absorption and lymph flow.

2. Tissue pressure is gauged by the resistance tissue offers to dilation of its interstitial spaces by edema fluid.

3. Tissue pressure is proportional to the density and elasticity of tissue and decreases as the tissue loses its elasticity.

4. The integument encompassing the skin and bone, also facial places resist an in-

PATIENT	DATE	SOURCE OF SPECIMIN	TOTAL PROTEIN GRAMS %	ALBUMIN GRAMS %	GLOBULIN GRAMS %	OSMOTIC PRESSURE mm H ₂ O at 20° C.	SPECIFIC PRESSURE	EOSINOPHILES	
								%	TOTAL COUNT
BRISTOW	5-12-65	PLASMA	6.9	4.31	2.59	320	47	21	
Balloons Inserted Polyps Removed	5-12-65	NASAL POLYPS	5.9	3.54	2.36	250	42		
EZER	5-13-65	PLASMA	8.1	4.94	3.16	400	50	0	55.5
Balloons Inserted	5-13-65								
Polyps Removed	5-13-65	NASAL POLYPS	5.8	3.26	2.54	230	41		
FREEDMAN	6-8-65	PLASMA	7.7	4.50	3.20	370	48	64	
	6-17-65	NASAL POLYPS	6.9	3.87	3.03	310	45		
KOKEL	8-11-65	PLASMA	6.7	4.17	2.53	320	46		388.5
Balloons Inserted	8-5-65								
Polyps Removed	8-5-65	NASAL POLYPS	6.7	3.90	2.80	300	44		
McVAY	4-23-65	PLASMA	7.3	4.22	3.08	340	46	5	
	4-29-65	NASAL POLYPS	7.1	3.94	3.16	320	44		
MIKUS	5-18-65	PLASMA	7.2	4.22	2.98	330	46	47	
	5-18-65	NASAL POLYPS	6.9	3.78	3.12	300	44		
MONTE	1-21-65	PLASMA	7.1	3.42	3.68	290	42	15	556.1
Balloons Inserted	1-13-65								
Polyps Removed	1-13-65	NASAL POLYPS	6.1	4.17	1.93	280	46		
SEBER	2-4-65	PLASMA	6.5	4.14	2.36	300	46	3	
	2-4-65	NASAL POLYPS	4.5	2.64	1.86	170	37		
TANNERY	2-2-65	PLASMA	7.1	4.22	3.08	340	46	5	399
	2-2-65	POLYP FLUID	5.0	3.14	1.86	200	40		
WHITMIRE	3-16-65	POLYP FLUID	5.9	3.55	2.34	260	44		
Balloons Inserted Polyps Removed	3-26-65	POLYP FLUID	5.3	3.53	1.77	230	43	20	350
	4-1-65	PLASMA	6.9	4.33	2.67	350	47		
	4-27-65	POLYP FLUID	6.5	3.69	2.81	280	43	10	
WILLIAMS	2-11-65	PLASMA	7.1	4.92	2.18	360	50		
	2-11-65	POLYP FLUID	5.3	3.79	1.51	230	43		
	3-4-65	POLYP FLUID	6.3	4.43	1.86	310	47		

This table records the relative values of the protein content derived by electrophoresis, and also the colloid osmotic pressure of the plasma and tissue fluid of patients with maxilloethmoidal polyposis. The values of colloidal osmotic pressure were found through the use of the nomogram of Wells, H. S., Youmans, J. B., and Miller, D. G., Jr. (J Clin Invest 12:1103, 1933).

crease in tissue pressure (walls of sinuses and walls of the nasal cavities).

5. Tissue pressure increases with the rate of dilation of the interstitial spaces and increases as these spaces become filled with fibroblasts.

6. Tissue pressure may be increased by application of physical pressure to the surface of the part.

Treatment

A very effective method of increasing the tissue pressure of the sinusal mucosa and reversing or retarding the progress of the pathology is to insert into the maxillary sinus an artificial polypus in the form of a balloon and to fill the balloon with iodized oil. As oil is added to the balloon it expands and increases the tissue pressure of the mucosa and promotes absorption of the edema fluids.²²

As this is accomplished, the weight of the heavy iodized oil displaces the sinusal secretion. By obliterating the sinusal cavity with an incompressible medium, the pulsations of the arterioles and dilated arteriovenous anastomoses are transmitted to the lymph vessels. This transmission produces absorption of the edema fluid and increases the flow of lymph-bringing agents from the blood (hormones?) which may neutralize the conglutinant^{9,15} in the tissue fluid and either allow the excretion into the nasal cavities of the proteins in the edema fluid or facilitate their passage through the semi-atrophic lymphatic system. McMaster has reported that pulsatile pressure produces an increase in lymph flow seven times greater than constant pressure even though the systole pressure was never greater than the constant pressure.^{8,9,10}

Indications

The indications for insertion of balloons into the maxillary sinuses are principally related to pathologic processes which cause retention of an excessive amount of tissue fluid in the mucosa of one or both of the maxillary sinuses. The capacity of the maxillary sinuses often equals the sum of the capacities of all of the other sinuses. Treatment directed only to the maxillary sinuses

often reduces the intranasal turgescence and promotes resolution of pathology in the other sinuses. This principle may be applicable to both allergic and purulent sinusitis or allergic sinusitis with secondary infection.

Bronchial asthma associated with maxillary sinusitis may often be relieved by insertion of balloons into the maxillary sinuses. This type of treatment has also been successful in helping to cure subacute and chronic purulent sinusitis, incipient bronchiectasis, perennial allergic rhinitis and certain types of otitis media with effusion which are associated with unilateral or bilateral latent purulent sinusitis.

Contraindications

Contraindications to insertion of balloons are any type of acute allergic or purulent rhinitis or sinusitis or acute bronchial asthma. Before insertion, a high leucocytosis or eosinophilia should be brought under control with steroid hormones and/or antibiotics. If this is not done, insertion of balloons may precipitate Löffler's or Harkavy's syndrome.

X-ray of the chest and an electrocardiogram are indicated in patients with high blood eosinophilia and reduced pulmonary function.

The writer has inserted balloons into the sinuses of about 500 patients without any serious complications. Most of the writer's patients have had their balloons in their sinuses for about three months. However, quite a number of them have insisted that the balloons be left in their sinuses for from six to eight months to one year.

Balloons are not inserted during the patient's hay-fever season and should not be removed during that season. If they are, the patient may have a severe attack of asthma. As oil is added to the balloons about every two or three weeks, newly formed polypi may present in the middle meatus. These may be removed without the danger of precipitating an attack of asthma if balloons are in the sinuses and are well inflated. In 1895 Semon²⁴ reported asthma following polypectomy.

The technique of insertion of balloons can be found in the articles listed in the author's bibliography.

Many of the writer's patients have been treated for allergy for years before balloons have been inserted into their sinuses. Obviously the insertion of balloons would not be necessary if the treatment for allergy prevented or caused the polypi to disappear. If a patient continues to take injections from an allergist after balloons are inserted into the maxillary sinuses, frequently the dosage must be reduced. If it is not reduced, the patient may have an episode of bronchial asthma following each injection. The writer usually insists that the patient continue his treatment for allergy.

Summary

The physiology and functional pathology

of the lymphatic system has been described as it is related to maxilloethmoidal polyposis. A method of treatment of maxilloethmoidal polyposis has been described and its indications and contraindications given. The possibility of the nasal and sinusal mucosa being an organ of excretion during pathologic states has been suggested.

Note: Author is grateful to Franz Leidler, M.D. and his associates at the Memorial Baptist Hospital Laboratories for the electrophoresis of plasma and tissue fluids.

The balloons used were made by C. R. Bard, Inc., Murray Hill, New Jersey. The size used most frequently were those containing 8 mm. or 10 mm. deformable heads.

References

1. Boies, L. R.: Fundamentals of Otolaryngology, Ed. 2nd. p. 205. W. B. Saunders Co., Philadelphia and London, 1954.
2. Thomson, Sir St. Clair: Diseases of the Nose and Throat, Third Edition, D. Appleton and Co., New York, MCMXXVI, p. 7, 8, 9, 201, 235.
3. Lacoarret, Rev. Hebd. de Laryngol.: XXII, II, No. 37, p. 333, 1902 (Quote from Thomson).
4. Drinker, C. K. and Yoffey, J. M.: Lymphatics, Lymph and Lymphoid Tissues. Harvard University Press, Cambridge, Mass., p. 24, 34, 52, 83, 147, 151, 158, 173, 282, 344-5, 1941.
5. Piersol, G. A.: Normal Histology. J. B. Lippincott, Philadelphia, Pa. 2nd Ed., p. 403, 1894.
6. Davison, F. W.: Hyperplastic Sinusitis, A Five Year Study. Ann Orl 72:462, 1963.
7. Davison, F. W.: Rhino-Bronchology. Laryngoscope 76:1300, 1966.
8. McMaster, P. D. and Kidd, J. G.: Lymph Nodes as a Source of Neutralizing Principle for Vaccinia. J Exp Med 66:73, 1937.
9. McMaster, P. D. and Hudack, S.: The Formation of Agglutinin within Lymph Nodes. J Exp Med 61:783, 1935.
10. Quoting from McMaster, P. D.: Lymphatic Participation in Cutaneous Phenomena. Harvey Lecture, April 16, 1942. Bull NY Acad Med p. 753, Nov. 1942.
11. Robison, J. M.: The Lymph Pump Mechanism of the Nose and Paranasal Sinuses. Laryngoscope 60:5:489, 1950.
12. Robison, J. M.: Subacute Catarrhal Otitis Media and Mastoiditis with Effusion. Southern Med J 35:9:815 and p. 7, Fig 6, 1942.
13. Dorland's Illustrated Medical Dictionary, Ed. 24, p. 58, 246, 690, W. B. Saunders Co., Philadelphia and London, 1965.
14. Remington, Jack S., Vosti, K. L., Lietze, A., and Zimmerman, A. L.: Serum Proteins and Antibody Activity in Human Nasal Secretions. J Clin Invest 43:8:1613, 1964.
15. Coombs, R. A., Coombs, Anne M. and Ingram, D. G.: The Serology of Conglutination. Blackwell Scientific Publications, Oxford, p. 3, 81, 194, 1964. Published in U. S. by Chas. C. Thomas.
16. Robison, J. M.: Lymphangitis of the Retropharyngeal Lymphatic System. Arch Otolaryng 40:385, 1944.
17. Complement, Ciba Foundation Symposium, Little Brown and Co., Boston, p. 5, 58, 242, 245, 272, 278, 1965.
18. Shioda, H., Mishima, T.: The Significance of Mast Cells in Nasal Smears from Patients with Food Allergy. J Allerg 37:6:321, 1966.
19. Rathbone, R. Rhett: The Roentgen Diagnosis and Therapy of Retropharyngeal Adenitis. Radiological Clinic of Drs. Groover, Christie and Merritt, Childrens' Hospital, Washington, D. C., 43: 1:25-40, Jan. 1940.
20. Yoffey, J. M., Courtice, F. C.: Lymphatics, Lymph and Lymphoid Tissue. Harvard Univ Press, Cambridge, Mass., p. 173, 223, 442, 448, 466, 243, 187, 371, 227, 440, 186, 229, 463, 242 table 34, 171, 237 table 32, p. 31, 1956.
21. Roviore, H.: Translated by M. J. Tobias, Glossary p. 275, 273:17, Edwards Brothers, Inc., Ann Arbor, Mich., 1938.
22. Robison, J. M.: Pressure Treatment of Allergic Sinusitis. Arch Otolaryng 45:405, 1947.
23. Robison, J. M.: Catarrhal Otitis Media with Effusion. Southern Med J 44:9:777, 1951.
24. Semon, F.: Brit Med J, Jan. 5, 1895, I, Quoted from Thompson, p. 201.
25. Wells, H. S., Youmans, J. B. and Miller, D. G., Jr.: J Clin Invest 12:1103, 1933.

When a man dies, he does not just die of the diseases he has: he dies of his whole life. — Charles Peguy

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I.M. administration; epinephrine effects may be reversed; dermatological reactions; parkinsonism-like symptoms on high dosage (in rare instances, may persist); weight gain; miosis; lactation and moderate breast engorgement (in females on high dosages); and less frequently cholestatic jaundice. Side effects occurring rarely include: mydriasis; agranulocytosis; skin pigmentation, lenticular and corneal deposits (after prolonged substantial dosages).

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Smith Kline & French Laboratories 

Management of Acute Suppurative Sinus Disease

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PRESENT DAY management of acute suppurative disease is conservative. The medical advances of the past few decades provide us with a better understanding of the disease processes and a more effective means of control. The diagnosis of acute sinusitis is not difficult if a careful history and examination is done.

Etiology

The role of allergy in preparing the stage for an acute infection is not completely understood, but many workers feel it is important. Also, many investigators feel that vitamin deficiencies, endocrine imbalances, poor environment, insufficient outdoor exercise, lack of proper humidity in artificially heated homes, prolonged exposure with chilling of the body surfaces, and fatigue may be predisposing factors. Anatomical defects such as adenoids, infected tonsils, or deviated septa are certainly important intrinsic factors, and any of these may provide suitable soil for subsequent bacterial invasion. Because of the cleaning action of the cilia the sinuses are sterile, even though bacteria may enter them. Anything that causes impairment of or absence of the cilia leads to a retention of bacteria and a predisposition to sinusitis.

Symptoms

Common symptoms generally are: malaise; tenderness over the involved sinus or pressure; headache worse in the morning and subsiding later in the day; nasal obstruction, a discharge, mucoid at the onset and becoming purulent later; and varying degrees of fever. Findings include nasal obstruction, uni- or bilateral, congested turbinates, and purulent or mucopurulent discharge. Roentgenograms and less often transillumination may confirm the diagnosis. Because of the possibility of an allergic factor, examination of the nasal secretions for eosinophiles is worthwhile.

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Treatment

In acute maxillary sinusitis, bed rest, promotion of drainage, sedation for pain, and indicated antibiotics based on culture and sensitivity studies, may be all that is needed; although, vasoconstrictor sprays and nasal suction, following the procedure of Proetz, can be very helpful. Patients who experience severe pain and have purulent discharge, or roentgenograms suggesting a delay in resolution, or inadequate drainage need additional treatment. In such cases, minor procedures such as infracture of the middle turbinate, turbinotomy of the anterior ends of the middle turbinates, or opening of the agger-nasi cell may be helpful in providing better drainage. If the x-ray shows a fluid level, puncture through the inferior meatal wall and irrigation of the maxillary sinuses are indicated. In persistent cases, however, it may be necessary to perform an intranasal antrostomy to provide sufficient drainage from the antrum.

Persistent acute maxillary sinusitis is an indication for intra-nasal antrostomy which may prevent the later formation of an antro-alveolar fistula. This procedure should be done through the lateral wall of the inferior meatus, by perforating the wall with a trocar and then enlarging it with biting forceps to get an opening of sufficient size. Care must be taken not to injure the orifice of the lacrimal duct, situated anteriorly, just under the overhanging inferior turbinate.

Acute frontal sinusitis is common in adults but rare in children. If frontal pain and tenderness over the sinus, edema of the upper eyelids, or clouding and fluid levels on x-ray persist, a trephine of the floor of the frontal sinus may be required. An incision should be made just inside the eyebrow on the mesial

side, the soft tissues elevated, and the sinus opened sufficiently to allow an insertion of a polyethylene tube. The tube should be left in place and daily irrigations of normal saline continued until the symptoms subside and the saline freely enters the nose.

While frontal sinusitis is rare in children, acute infections of the ethmoids and antra are at times encountered. Conservative measures usually are effective unless there has been a delay in seeking treatment, in which case the possibility of orbital abscess must be kept in mind. Acute suppurative sphenoiditis is rare and is usually an acute exacerbation of a chronic infection.

Orbital abscess, secondary to ethmoiditis, should be drained externally, using the conventional approach for the external ethmoidectomy operation. The orbital periosteum is elevated posteriorly and the orbit decompressed. This may require ligation of the anterior ethmoid artery, or it may be controlled by the use of a small metal clip such as used by the neurosurgeon. Occasionally, where there is marked swelling of the lids, secondary incisions through both the upper and the lower lids and the insertion of a rubber drain may be indicated.

Conclusions

Acute suppurative sinusitis usually responds to conservative management unless complicated by pre-existing factors or delays in obtaining treatment. The use of antibiotics, based upon culture and sensitivity studies, will eliminate most of the complications formerly encountered. Advantage should be taken to suggest correction of significant intrinsic or extrinsic factors aimed at the prevention of future attacks, and on occasion, special operative procedures are required to alleviate severe or persistent symptoms.

Evolution

The karygranulomes, not the idiogranulomes or microsomenstratum in the protoplasm of the spermatogonia, unite into the idiosphacrosome, acrosoma of Lenhossék, a protean phase, as the idiophacrosome differentiates into an idiocrytosome and an idiocalyptosome, both surrounded by the idiophacrotheca, the archoplasmic vesicle; but the ideoctosome disappears into the metamorphosis of the spermatid into a sphere, the idiophtharosome. — William Osler

Sensori- Neural Hearing Loss

Its Nature and Etiology

THEO. E. WALSH, M.D.*
St. Louis, Missouri

SENSORI-NEURAL HEARING loss may be either congenital or acquired. Congenital sensori-neural hearing loss may be on a developmental basis or may be the result of Rh incompatibility and kernicterus, maternal rubella in the first trimester of pregnancy, anoxia and viral infections.

Congenital sensori-neural hearing loss is usually bilateral and severe. It is noticed by the parents when the child is quite small and fails to respond in the usual way to loud sounds and also fails to acquire speech. The parents are greatly disturbed and need the physician's sympathetic attention. Although there is nothing medical that can be done for this type of hearing loss, training in speech, the use, by means of hearing aids, of any residual hearing that may be present, and special schooling are essential. The parents should be advised that these children frequently have a high I.Q. and with proper schooling will learn to communicate and become useful citizens. They should be in a special school early, ideally at the age of three years.

The acquired sensori-neural hearing loss may be the result of: (1) acoustic trauma, (2) degenerative changes, (3) head trauma, (4) heredity, (5) infections, (6) Meniere's disease, (7) ototoxic drugs, (8) tumors of the eighth nerve and (9) vascular accidents.

In the diagnosis of sensori-neural hearing loss the tuning fork is the most useful tool. If the patient hears better by air conduction than by bone conduction the hearing loss is sensori-neural. In the examination of such patients a pure-tone audiogram is a useful record of his hearing and establishes the threshold of his hearing at the various frequencies at which he is tested. He must be tested both by air and by bone conduction. A speech audiogram, i.e., a test of the patient's ability to hear and understand speech, is essential if we are to be able to advise

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him whether he can be helped by hearing aids or other means. Although the average of the patient's threshold at the speech frequencies on the pure-tone audiogram is indicative of his speech reception threshold, the pure-tone audiogram tells us nothing of his ability to understand speech when it is delivered at a sufficient intensity above his threshold. In this test, a list of phonetically balanced monosyllabic words is presented to the patient at approximately 40 decibels above his speech reception threshold. His discrimination score is the percentage of words repeated correctly. In sensori-neural deafness the discrimination score is always markedly reduced.

Acoustic Trauma

Individual sensitivity to loud sounds varies considerably. Exposure to excessively loud noise as in industry (boilermakers, drop-forge workers, etc.) or to repeated insults, such as gunfire, leads at first to a temporary threshold shift. The patient exposed to such loud sounds complains first of a tinnitus and an inability to hear. If no further exposure is experienced the hearing may return to normal. Repeated exposure causes permanent damage. The pure-tone audiogram shows a loss at 4,000 cycles. As time goes on the loss may spread for both the high and the low tones but is usually most severe at the 4,000 cycle tone. Such loss is usually bilateral and progressive.

Degenerative Presbycusis*

The hearing loss of presbycusis occurs in the older age groups and is probably the most common type of acquired sensori-neural hearing loss with which we have to deal. In presbycusis the pure-tone audiogram shows a sharp drop in the high tones, usually 2,000 cycles and above, and is slowly progressive. In the earlier stages the speech reception threshold is not greatly impaired. The discrimination for speech, however, is greatly impaired. Such patients complain that they hear but do not understand. They are particularly bothered by ambient noise and hear and understand poorly in a noisy environment but fairly well when

speaking vis-a-vis in a quiet room. It is obvious that with a good speech reception threshold and poor discrimination a hearing aid would be useless. Whenever the speech reception threshold deteriorates to 40 decibels or worse, a hearing aid may be justified. The patient, however, should be instructed that it is difficult to become accustomed to this aid and that he will have to persevere in the use of it.

Head Trauma

A blow of the flat of the hand on an ear, an explosion near the ear, or sometimes an inexperienced dive when the ear hits flat against the water may cause a rupture of the tympanic membrane and give rise to a conductive deafness. At the same time great trauma is done to the cochlea by this excessive pressure and a sensori-neural deafness occurs. This may also happen with a blow on the side of the head, usually with a flat object. The hearing loss in such cases is sudden, usually unilateral, and may be total.

Heredity

Not infrequently one sees a patient with either a unilateral or a bilateral hearing loss of any severity who gives a history that the parent, grandparent and great-grandparent all acquired such a hearing loss at the same age. Total congenital hearing loss may be hereditary. Hereditary hearing loss manifesting itself in the teens is usually more in the high tones, spreads rapidly, and may become total.

Infections

Various degrees of sensori-neural deafness may be acquired after attacks of viral infections such as mumps, measles, flu, etc. The loss may be bilateral or unilateral, may be of any degree, and is not usually progressive.

Meniere's Disease

Although Meniere's disease is primarily a cochlear disease the patient usually presents himself complaining of acute vertiginous attacks. In obtaining a history of such an attack one can usually elicit the fact that it is accompanied by a roaring tinnitus in one ear, sensitivity to loud sounds and difficulty

*See Test Your Word Score Page 1028.

in hearing. The classical triad of Meniere's disease is therefore a roaring tinnitus, vertiginous attacks and sensori-neural deafness. In testing such patients we find in the early stages that the low tones are more affected as a rule than the high. The patient is peculiarly sensitive to loud sounds. The same tone applied to each ear will be heard differently in the two ears (diplacusis). Hearing in such cases fluctuates and during remissions may be perfectly normal. As time goes on, however, the hearing becomes gradually worse and finally is quite useless. Although in many cases the speech reception threshold is not greatly impaired, the discrimination score is always markedly poor. In the early stages, medical therapy may be of great value in preserving the hearing and controlling the vertiginous attacks. When, however, the hearing has deteriorated and does not fluctuate, medical therapy is of no avail. It is fortunate that Meniere's disease is more commonly unilateral than bilateral.

Ototoxic Drugs

The administration during infections of such drugs as dihydrostreptomycin, kanamycin, quinine, etc., has caused severe sensori-neural hearing loss. This is rapidly progressive with the antibiotics and may be total. Excessive use of aspirin may cause some temporary sensori-neural hearing loss; but

hearing usually improves when large doses of aspirin are discontinued.

Eighth Nerve Tumors

The hearing loss in tumors of the eighth nerve is slowly progressive. The patient usually complains early of a tinnitus and sometimes of an inability to understand speech, although he can frequently hear it. Tumors of the eighth nerve usually arise on the vestibular division of the nerve and affect the cochlear division by gradual, increasing pressure. Unless the tumor is recognized and removed early the loss may be total.

Vascular Accidents

Occasionally sudden loss of hearing is experienced in one ear. The explanation for such sudden total hearing loss is usually presumed to be a hemorrhage into the inner ear or some central nervous vascular accident.

Summary

Sensori-neural hearing loss may be congenital or acquired. Although with the possible exception of Meniere's disease medical therapy is of little avail in improving the hearing loss, the physician can serve a very useful purpose in advising those afflicted with sensori-neural deafness in the use of hearing aids, education, etc.

Green Medicinals Herbs for the Throat

Ecclesiasticus said: The Lord hath created medicines out of the earth and a wise man will not abhor them. Medicinal herbs for the throat include black currant leaves, columbine, hedge mustard, knapwood, quinsywort, rampion, throatwort, violets, and yellow dock, yielding gargles, syrups, and tonics.

A tempting ice can be prepared from the leaves and shoots of the black currant tree:

Black Currant Tree Ice

Take two or three handfuls of young black currant leaves and shoots and throw them into a saucepan with four cups of boiling water — add a pound of sugar and the juice of two lemons and mix well. Let it boil three times, then pass the mixture through a sieve and allow it to cool — when lukewarm add a tablespoon of gelatine and pour into a mould and freeze.

— C. F. Leyer: Green Medicine

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*Based on Statistical Report, U.S. Dept. Commerce, ed. 86, and Fisher, G. F., and Vavra, H. M.: Pub. Health Rep. 80:961 (Nov.) 1965.

Note: DEXTROSTIX is not meant to replace the more precise analytical laboratory procedures such as needed in glucose tolerance testing.

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Ames

Acoustic Tumors

Diagnosis and Management

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FOR REASONS WHICH are not known, the acoustic nerve is the most common site of benign neuromas in the body. Acoustic tumors are believed to arise from the Schwann cells of the nerve sheath and are more properly called "Schwannomas."¹ Although they are benign and slow growing, their location when enlarged in the posterior fossa, next to the brain stem, makes them a serious death-dealing lesion.

The first successful removal of an acoustic neuroma was accomplished by Sir Charles Ballance in 1893.² To Harvey Cushing goes credit, however, for alerting the medical profession to the problem of acoustic tumors and for standardizing the surgical approaches to these lesions. The monograph, *Tumors of the Nervus Acousticus and the Syndrome of the Cerebellopontine Angle*³ published in 1917 by Cushing, reported on 30 cases approached through a suboccipital craniotomy. Each of these cases was far advanced by today's standards, all of these patients having severely elevated intracranial pressure, and half of them being afflicted with varying stages of blindness as a result of prolonged elevated intracranial pressure. By 1917 Cushing was able to lower the mortality of acoustic tumor surgery from an appalling 80 percent to a much more acceptable 30 percent. This was accomplished by wide decompression of the posterior fossa and extensive subtotal enucleation of the interior of the tumor. In most instances he felt that a total removal of this tumor was not possible.

Since 1917, tremendous strides in the diagnosis and management of these lesions have occurred. Otolaryngologists, neurosurgeons and neurologists have contributed generously to these advances. It remains, however, for an alert medical community to suspect this tumor in its early stages if the advances

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From the Otologic Medical Group and sponsored by the Los Angeles Foundation of Otology.

that have occurred will, indeed, be made available to these patients.

Diagnosis

The adaptation of microsurgical technique for the removal of acoustic tumors has made the diagnosis of these lesions while they are still small more than an academic exercise.⁴ Accordingly it will be the purpose of this section to emphasize those diagnostic features which may be detected early in the history of this tumor. Our discussion will summarize the abnormalities found in the following areas of diagnosis: clinical, audiologic, vestibular, radiologic, and neurologic.

Clinical

Acoustic tumors may occur in any age group. They are most commonly seen, however, in the 4th and 5th decades of life. There is no sex dominance.

The earliest symptoms are caused by disturbances of the 8th cranial nerve in both its vestibular and auditory branches. Tinnitus may be high-pitched and persistent. Hearing loss is insidious in onset and then progressive. While the tumor is small these patients have difficulty in understanding the meaning of words, rather than in the actual perception of sound. As the tumor enlarges, however, perception of sound also deteriorates.

Unsteadiness is commonly seen. This will be more pronounced on rapid positional change and under conditions of anxiety or fatigue. The unsteadiness is generally of brief duration. Over a period of time most patients compensate for it. Many patients who are seen in the late stages of their disease will have forgotten about it.

True vertigo, similar to that seen in Meniere's disease, has been found in 25 percent of our cases.

Pain and dysesthesias in the external auditory canal or behind the ear over the mastoid may be present.⁵ These sensory disturbances are felt to be due to pressure on the sensory portion of the seventh cranial nerve (*nervus intermedius*).

As the tumor enlarges and grows out into the posterior fossa, symptoms of an intra-

cranial neoplasm become apparent. The patient may complain of headache, difficulty with gait, visual impairment, ocular palsies, facial weakness, numbness and difficulty swallowing.

Audiologic

Acoustic tumors usually develop on the vestibular portion of the auditory nerve in the internal auditory canal. As the tumor enlarges, it causes pressure on the adjacent cochlear division. This results in abnormal audiologic function.

Tuning fork tests, tests of pure tone reception, speech discrimination, auditory fatigue, and loudness function, help to localize the retrocochlear site of the tumor.⁶

TUNING FORK TESTS

Patients with acoustic neuromas will show lateralization of the tone to the normal ear. Air conduction will be heard greater than bone conduction on the affected side. When the difference in hearing is marked between the two sides, masking of the normal ear must be carried out for tuning fork tests to have validity. A Barany noisemaker suffices very well for this purpose.

PURE TONE AUDIOGRAM

The patient with an acoustic tumor will show a sensori-neural type hearing impairment with the most pronounced loss being in the higher frequencies. A high-frequency loss has been found in 70 percent of our cases.

SPEECH DISCRIMINATION

The ability to understand the meaning of words is one of the earliest audiologic parameters to be affected by acoustic tumors. Speech discrimination measured by standard phonetically balanced word tests will show marked impairment. This is in contrast to patients with a conductive impairment and normal hearing patients who will show high discrimination. Patients with cochlear lesions, such as Meniere's disease, will occasionally show a moderate impairment in speech discrimination.

AUDITORY FATIGUE TESTS

Patients with normal hearing, or those with a conductive impairment, are able to hear continuous tones presented just above threshold for a prolonged period of time without developing significant auditory fa-



Fig. 1 — Iophendylate study of the posterior fossa showing defect in the contrast column adjacent to the right internal auditory meatus.



Fig. 2 — Middle fossa (subtemporal) approach to the roof of the internal auditory canal. Self-retaining retractor is in place elevating the dura overlying the temporal lobe. The internal auditory canal is exposed on the floor of the middle fossa.

tigue.

In sensori-neural impairment a varying amount of adaptation, or auditory fatigue, will occur, depending upon the location of the lesion. Auditory fatigue is minimal and usually limited to the higher frequencies in cochlear disorders. In cases of acoustic neuroma, there may be severe or total adaptation, as measured by the modified tone decay test or Bekesy Audiometry. In this latter test, the Type III and Type IV curves are characteristically seen.⁷

LOUDNESS FUNCTION TESTS

Patients with retro-cochlear lesions have normal responses to loudness function tests such as the alternate binaural loudness balance test and the short increment sensitivity index test. In contrast to this, abnormal responses are found in patients with cochlear lesions.

Vestibular

Testing the labyrinth with ice water will show hypoactivity in approximately 90 percent of patients.⁸ Of this group, 50 percent will have a functionless labyrinth.

Spontaneous nystagmus may be variable. In the early stages of this disease, it is often not found. An electronystagmograph can be used to detect spontaneous nystagmus which may not be apparent on clinical examination.

Radiologic

Carefully taken plain x-rays, including Stenver's projection, will show a difference in the diameter between the auditory meati. A difference of 1 millimeter is suspicious if this is accompanied by erosion or a difference in the shape of the two internal auditory canals.⁹

Positive contrast studies of the posterior fossa using iophendylate have increased the accuracy of radiologic diagnosis of these tumors to 95 percent. The tumor defect appears as an indentation in the iophendylate medium at the porus acousticus¹⁰ (Figure 1).

Neurologic

There are several tests which can be read-

ily carried out by the otolaryngologist and general practitioner in his office that will be very helpful in making the diagnosis of acoustic neuroma. Testing of the corneal responses can be done with a small wisp of cotton. The corneal response is one of the first neurologic reflexes to be blunted by an acoustic tumor.¹¹ In addition to this, testing the sensation along the posterior aspect of the external auditory canal will very often show impairment in these patients. This test can be performed with a blunt right angle hook.⁵

Spinal fluid protein is generally not elevated while the tumor is confined to the internal auditory canal, or only slightly protruding into the posterior fossa.¹² Elevation does occur, however, to a marked degree as the tumor enlarges and indents the adjacent brain stem.

Treatment¹³

The treatment for acoustic tumors is surgical with few exceptions due to severe infirmities or far-advanced age.

The goal of surgery should be total removal of the tumor within the framework of the following criteria:

1. Avoidance of further cranial nerve damage.
2. Adequate decompression of the posterior fossa.
3. Avoidance of injury to the brain stem or cerebellum.
4. Satisfactory access for removal of the tumor and management of any postoperative complications.

The operations that are in use today are of four types: (1) middle fossa approach, (2) translabyrinthine approach, (3) suboccipital approach, (4) combined suboccipital-petrosal approach (trans-sigmoid approach).

Middle Fossa Approach

The middle fossa approach (Figure 2) is a surgical technique designed to remove tumors confined to the internal auditory canal. This limited approach is indicated for small tumors only when hearing preservation or improvement is possible. It is accomplished

through a sub-temporal craniectomy with elevation of the temporal lobe of the brain. The internal auditory canal is exposed from above and removal of small tumor in the canal is carried out.

Translabyrinthine Approach

The translabyrinthine approach (Figure 3) is a direct surgical route through the mastoid and labyrinth to the cerebellopontine angle. It is used for removal of tumors of moderate size not associated with elevated intracranial pressure and not extending below the level of the jugular bulb. The facial nerve is identified early in the dissection prior to extensive tumor removal, allowing its preservation in most instances.

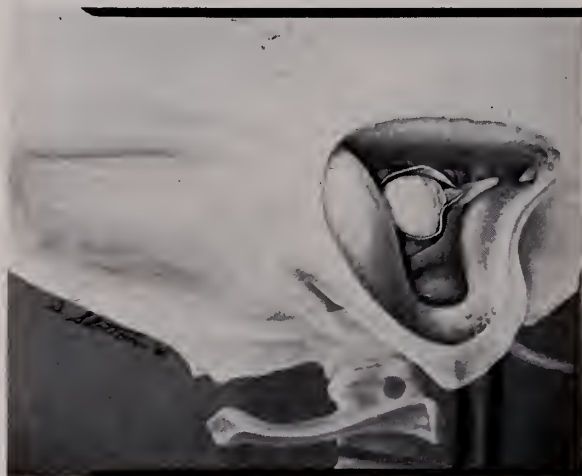


Fig. 3 — Translabyrinthine approach to the cerebellopontine angle. Tumor is visible beneath the cut dura lying above the jugular bulb. The facial nerve has been exposed in the internal auditory canal.

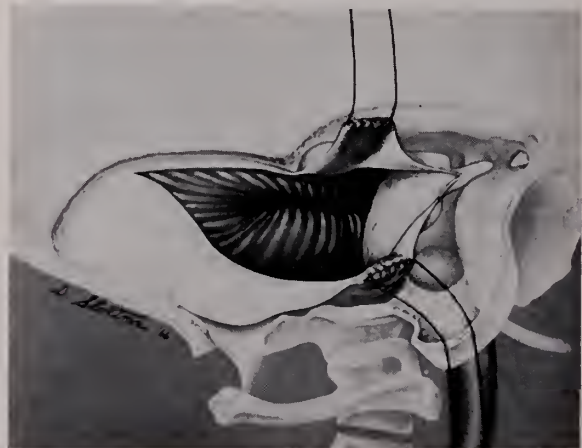


Fig. 4 — Combined approach to the cerebellopontine angle. In this case the sigmoid sinus has been divided.

Suboccipital Approach

The suboccipital approach to the cerebellopontine angle is carried out by removal of a portion of the lateral suboccipital bony plate. The intervening lateral cerebellar hemisphere is either reflected or partially resected in order to allow access to the tumor. This operation has been widely accepted in the past as the standard approach for all tumors in the cerebellopontine angle. It continues to be an excellent approach for large tumors.

*Combined Suboccipital-Petrosal Approach
(Trans-sigmoid Approach)*

The combined suboccipital-petrosal approach (Figure 4) to the cerebellopontine angle is carried out by extending the suboccipital bony opening forward over the sigmoid sinus to the internal auditory canal. The sigmoid sinus may be either ligated and divided or mobilized depending on the situa-

tion of the tumor. This operation allows wide decompression of the cerebellopontine angle, direct access to the tumor, and early exposure of the facial nerve. The dura overlying the cerebellum is kept intact in order to prevent operative injury to this structure.

Summary

It is only through a thorough understanding of the early changes that occur in patients with acoustic tumors and persistence in the evaluation of these challenging patients that we will be able to make this diagnosis while the tumor is still small. At this stage of its growth, it is most susceptible to eradication with a minimum of residual neurologic deficit.

The early changes caused by an acoustic tumor have been reviewed in relation to clinical, audiology, vestibular, radiologic, and neurologic aspects. Most of these diagnostic procedures can be carried out by the practicing physician in his own community.

References

1. Dykstra, P. C.: The Pathology of Acoustic Tumors. *Arch Otolaryng* 80:605, 1964.
2. Ballance, C.: Some Points in Surgery of Brain and Its Membranes. London: Macmillan & Co., p. 276, 1907.
3. Cushing, H.: Tumors of Nervus Acusticus and Syndrome of Cerebellopontine Angle. Philadelphia: A. B. Saunders Company, 1917.
4. House, W. F.: Transtemporal Bone Microsurgical Removal of Acoustic Neuromas. *Arch Otolaryng* 80:597, 1964.
5. Hitselberger, W. E., and House, W. F.: Acoustic Neuroma Diagnosis: External Auditory Canal Sensation As An Early Sign. *Arch Otolaryng* 83:218, 1966.
6. Johnson, E. W., and Sheehy, J. L.: Audiological Aspects of the Diagnosis of Acoustic Neuromas. *J Neurosurg* 24:621, 1966.
7. Jerger, J.: Bekesy Audiometry in Analysis of Auditory Disorders. *J Speech Hearing Res* 3: 275, 1960.
8. Pulec, J. L., and House, W. F.: Vestibular Involvement and Testing in Acoustic Neuromas. *Arch Otolaryng* 80:677, 1964.
9. Crabtree, J. A., and House, W. F.: X-ray Diagnosis of Acoustic Neuromas. *Arch Otolaryng* 80: 695, 1964.
10. Scanlan, R. L.: Positive Contrast Medium (Iophendylate) in Diagnosis of Acoustic Neuromas. *Arch Otolaryng* 80:698, 1964.
11. Pulec, J. L., and House, W. F.: Trigeminal Nerve Testing in Acoustic Tumors. *Arch Otolaryng* 80:681, 1964.
- 12-13. May be secured from the author or the reprints.

Medieval Remedy for Dysentery

Against dysentery, a bramble of which both ends are in the earth, take the nether root, delve it up, cut nine chips with the left hand and sing three times the Miserere Mei Deus and nine times the Pater Noster; then take mugwort and everlasting, boil these worts and the chips in milk until they get red, then let the man sip at night fasting a pound dish full, let him rest himself soft and wrap himself warm; if more need be let him do so again; if thou still need do it a third time thou wilt not need oftener.*

*Rapport, Samuel and Wright, Helen: *Great Adventures in Medicine*. The Dial Press, New York, 1952, p. 92.

Medicine is a science, acquiring a practice an art. — Anonymous



I'm supposed to get up and do things?

With my heart?

It's entirely natural—and may even be desirable—for the cardiovascular patient to be somewhat anxious about himself.

But when anxiety leads to unreasonable self-imposed limitations and restrictions . . . when it aggravates cardiovascular symptoms . . . when it interferes with restful sleep, measures to help alleviate the anxiety are probably in order.

One measure, of course, is reassurance. Another, adjunctive measure, is EQUANIL (meprobamate).

Over a decade of experience has shown that EQUANIL (meprobamate) is generally well tolerated as well as effective. Side effects are usually limited to transient drowsiness; serious, therapy-interrupting side effects are rare.

Cautions: Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use may result in dependence or habituation in susceptible persons—as ex-addicts, alcoholics, severe psychoneurotics. After prolonged high dosage, drug should be withdrawn gradually to avoid possibly severe withdrawal reactions including epileptiform seizures. Side effects include drowsiness and, rarely, allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute non-thrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. Meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angioneurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Warn patients of possible reduced alcohol tolerance. Should drowsiness, ataxia, or visual disturbances occur, dose

should be reduced. If symptoms persist, patients should not operate vehicles or dangerous machinery. A few cases of leukopenia, usually transient, have been reported following prolonged dosage. Other blood dyscrasias—aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis and hemolytic anemia—have occurred rarely, almost always in the presence of known toxic agents. One fatal case of bullous dermatitis following intermittent use of meprobamate with prednisolone has been reported. Prescribe very cautiously for patients with suicidal tendencies. Suicidal attempts should be treated with immediate gastric lavage and appropriate supportive therapy.

Contraindications: History of sensitivity to meprobamate.

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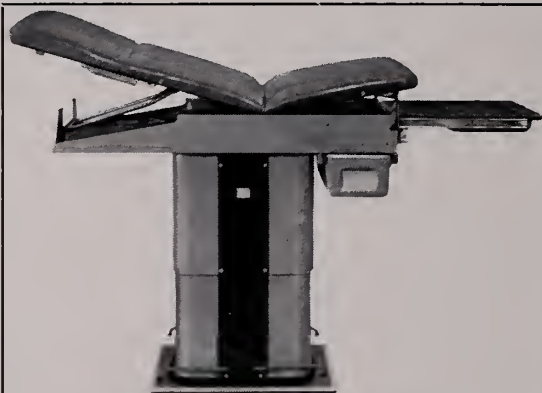
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Transsphenoid Hypophysectomy

WILLIAM W. MONTGOMERY, M.D.*
Boston, Massachusetts

THE TRANSPHENOID approach to the pituitary allows for a lower morbidity and mortality rate as compared with the anterior craniotomy route. There is less chance for injury to the optic chiasm. Postoperative complications such as seizures, extradural hematoma, brain damage, and cerebral edema are rare. The convalescent period following the transsphenoidal route for hypophysectomy is usually quite short.

There are a number of routes and modifications for the transsphenoidal hypophysectomy.

Operative Routes

Trans-Septal-Sphenoidal Hypophysectomy

This operation was pioneered by Oscar Hirsch in 1910. Cushing (1912) later used a sublabial modification of this route. Heck (1960) was the first in this country to use the transseptal approach for the treatment of advanced carcinoma of the breast. The main objection to this route is that it is a long narrow approach. Two instruments cannot be used simultaneously, and the dissecting microscope cannot be employed. It is, however, still used by many surgeons because of its being a direct midline dissection.

Transantroethmoidosphenoidal Hypophysectomy

Hamberger (1961) used this approach in a large series of patients with remarkable success. For most surgeons this is a long oblique route to the hypophyseal fossa. It also has the disadvantage of increasing the hazard of postoperative infection, for the oral route in some cases is potentially a septic area.

Transnasal Osteoplastic Hypophysectomy

Macbeth (1962) devised a unique direct midline approach using an osteoplastic skin flap based at the root of the nose. The only

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disadvantage here is that it leaves undesirable scarring of the nasal bridge. Those who perform this operation, however, indicate that this is not a factor when treating advanced carcinoma of the breast.

Transethmoidosphenoidal Hypophysectomy

This technique for hypophysectomy has been used since the turn of the century. Chiari in 1912 described this method for the removal of a pituitary adenoma. A few of the otolaryngologists who deserve credit for improving the techniques for this approach are Nager (1940), Bateman (1962), and James (1964). They have used this operation because it is the shortest route to the hypophysis with a wide field. It permits easy manipulation of instruments, and more than one instrument can be used simultaneously. One instrument may be inserted by way of the nasal cavity and another by way of the operative field. The advent of the surgical microscope has also increased the popularity of the transethmoidosphenoidal hypophysectomy.

The *transethmoidosphenoidal* approach for hypophysectomy has been used for solid and cystic pituitary tumors, palliative therapy for advanced breast carcinoma, diabetic retinopathy, and advanced prostatic carcinoma. Cystic tumors can easily be marsupialized. Solid tumors can be resected and/or decompressed. Most authors, Riskaer (1961) and Bateman (1962), for example, report 60% to 80% transient remissions when treating generalized metastases from carcinoma of the breast with hypophysectomy. Patients with breast carcinomatosis so weak that they could hardly turn in bed have had dramatic results following hypophysectomy. Similarly good results were obtained after hypophysectomy for diabetic retinopathy.

Preoperative Management

A team consisting of a neurologist, an endocrinologist, and a surgeon is essential for the proper management of the patient during the preoperative and postoperative periods. A rhinologist who attempts a hypophysectomy without the assistance of these two specialties is only inviting disaster. If

neurological and endocrinological work-ups have not been carried out prior to the patient's admission to the hospital, he should be admitted several days prior to surgery so that these may be accomplished. The neurologist will conduct a careful neurological survey which, in the case of pituitary tumors, should include radioactive scanning, pneumoencephalogram, and arteriograms. The endocrinologist will obtain the preoperative endocrine balance and prescribe the necessary hormones during the preoperative, operative, and postoperative periods.

Procedure

A complete external ethmoidectomy is performed. It is most important that the patient's head be secured in a supine position with the aid of sandbags. A septal mucosal flap is constructed before entering the anterior wall of the sphenoid. This flap is reflected into the nasopharynx in readiness to cover the defect in the posterior wall of the sphenoid sinus upon completion of the hypophysectomy.

Entering the Sinus

The right sphenoid sinus is entered and the entire anterior wall removed. The bony nasal septum is left intact as an accurate guide to the midline. On the other hand, a small portion of the posterior nasal septum may be removed for a wider exposure, without destroying its usefulness as a midline guide.

Dissecting Microscope

The dissecting microscope is employed for the remainder of the operation. The bulge of the sella turcica can be seen on the posterior wall of the sphenoid sinus. The midline is again checked by using the posterior aspect of the nasal septum as a guide. If the anatomical relationships are doubtful, x-rays may be taken with a portable machine using metallic probes as pointers or lead-shot attached to suture material.

Entering the Dura

A small opening is made in the posterior wall of the sphenoid (anterior wall of the

sella turcica) with a curette or a rotating burr. This is enlarged by using various rongeurs. Either a vertical or a cruciate incision is made in the dura; the pituitary or tumor thereof is then removed by using suction and various dissectors.

Closure of the Defect

Following the completion of the pituitary surgery, the fossa is packed with gelfoam saturated with thrombin solution if there is any bleeding or spinal fluid leakage. Muscle

or adipose tissues may also be used for this same purpose. The septal mucosal flap is elevated from the nasopharynx and reflected into the cyst cavity rather than used to cover the defect in the posterior wall of the sphenoid sinus. This is done to ensure marsupialization of the cyst. A single layer of absorbable gelatin sponge is placed on the flap prior to its being packed in place with iodoform gauze which has been impregnated with chlortetracycline ointment. The packing is removed on the fifth postoperative day.

Celsus* Eponyms

Celsus is notable for the classic description of inflammation, familiar to every medical student: redness, swelling, heat and pain (rubor et tumor, cum calore et dolore). His reference to "pus discharging from the ear, leading to insanity and death," is an early recognition of meningitis. His "distemper seated in the large intestine principally affecting that part where I mentioned the caecum to be, accompanied by violent inflammation and vehement pains, particularly in the right side," is an unsurpassed description of a disease which was supposed to be discovered in modern times — appendicitis. He was the first to mention that a vessel may be ruptured within the cranium, without fracture or depression; the first to use such terms as heart disease (cardiacus) and insanity (insania), and the first to describe circular amputation by a single sweep of the knife. He considered amputation "the last sad remedy," permissible only in gangrene; circular amputation is still known as Celsus' operation.

Other eponyms are in dermatology, for Celsus described forty skin diseases: severe acute papular eczema is called Celsus' papules, anesthetic leprosy is Celsus' vitiligo, the soft chancre is known as Celsus' chancre, suppurating ringworm of the scalp is known as Celsus' kerion, and the ever-famous condition of patchy baldness (alopecia areata) is not less distressing because it bears the classic name of Celsus' area. He was a pioneer in the history of medicine, and in such diverse fields as dentistry, laryngology, ophthalmology, lithotomy and plastic surgery — reparative work was needed by those Jews who wished to hold office among the Romans and could not do so if they lacked a prepuce.**

*Celsus (25 B.C.-50 A.D.)

**Victor Robinson: *The Story of Medicine*.

Pliny on Warts

Lie on your back along a boundary line on the twentieth day of the moon, and extend the hands over the head. With whatever thing you grasp when so doing rub the warts, and they will soon disappear.

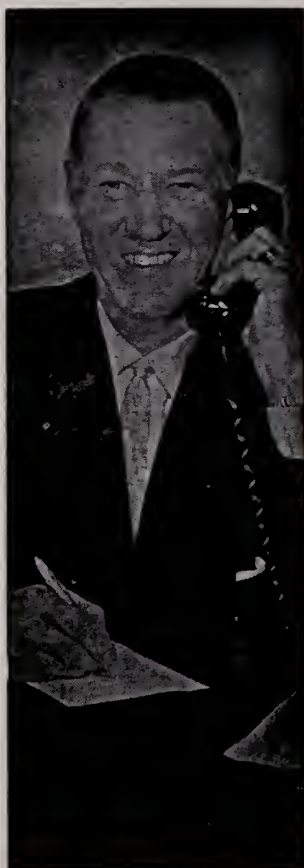
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Pharyngo- Tubo- Tympanic Disease

Management of

PHILIP E. MELTZER, M.D.*
Boston, Massachusetts

THERE IS A general impression that patients suffering from tubotympanic disease are on the increase, particularly patients with so-called "secretory ear" of various types. There are many good reasons why this may be so. The principle reason is that there is much better general understanding of the condition so that the correct diagnosis is made more frequently. This condition existed in the past but the symptoms were generally ignored, particularly in the "secretory ears" in young children.

Acute Suppurative Otitis Media

In the era before the sulfonamides and antibiotics, a child with an upper respiratory infection who developed pain in the ear usually developed an acute suppurative otitis media. The drum membrane would either rupture spontaneously or would have to be opened. With nothing to assist the child other than ear drops and a nasal spray, it was not surprising that "secretory otitis" was much less common than acute suppurative otitis media. The mechanics of effusions in the middle ear have been well known by the otologist for over seventy-five years. This was not true, however, of the general medical fraternity, including pediatricians and general practitioners. In fact, there were not too many practitioners in the 1915-1940 era who were able to see a drum membrane well enough to determine what was behind it. This remark is no reflection upon their ability as physicians, as the diagnosis of tubotympanic disease was not generally taught. Before the sulfonamides and antibiotics the focus was on acute suppurative otitis media. But in the last two decades there has been a complete change as far as the pediatrician and practitioner are concerned; they are now well able to diagnose other middle ear conditions by otoscopy.

*Posthumous. Clinical Professor Emeritus Otolaryngology, Harvard Medical School, 1961.

Nasopharynx and Eustachian Tube

A person with a normal functioning eustachian tube should be able to equalize the air pressure in the middle ear as against that of the outer atmosphere. Every time the palate is in motion, as in the act of swallowing, talking, yawning, the tube opens and closes, thus permitting air to enter and leave the middle ear. When, for one reason or another, the mucosa of the nasopharynx and eustachian tube becomes edematous, the swelling shuts off the airflow to the middle ear. The cause of the tubal obstruction may be hypertrophied adenoid, infection, or allergic edema with or without infection. If the tube is completely or partially occluded, symptoms such as a sense of fullness, tinnitus and slight deafness will result. If infection is the cause of the tubal obstruction and the infection extends to the middle ear, a more aggravated condition results. Pain occurs and the fluid in the middle ear changes in character to exudate.

Tubal Obstruction

The three most common causes of tubal obstruction are:

1. Infection of the mucous membrane in the nasopharynx.
2. Allergy.
3. Mechanical obstruction due to hypertrophied adenoid (particularly in children).

INFECTION

There are other causes, however, such as nasopharyngeal tumor, but the above three are most numerous. In children, the most frequent cause is the adenoid. Because of size this may be a purely mechanical obstruction. In these patients, relief is best accomplished by the thorough removal of the adenoid, particularly from the region of the fossa of Rosenmueller, the space just behind the torus of the tube, and from the torus of the tube itself. Despite thorough removal of the nasopharyngeal lymphoid tissue, recurrences are not uncommon. Susceptibility to middle ear conditions is an individual consideration, as not every child responds to nasopharyngeal infections in the same way.

Some children never have middle ear problems of any kind, yet have a huge adenoid, an allergy, and frequent postnasal infections. Other children have a small or no adenoid, yet their reaction to even the mildest infection is immediate tubal obstruction and blocked ears. This is also true in some adults. In many patients there is a strong family predilection related to inherent anatomic and physiologic factors.

ALLERGY

Allergic reaction of the mucosa in the middle ear and eustachian tube can occur as a part of an upper respiratory allergic state. In allergic children with nasopharyngeal infection the tissues respond poorly to treatment. On the other hand, treatment generally is quite effective in children with normal mucosa. The tissues in allergic children are already slightly edematous and when infection is superimposed upon their allergic membrane the edema is excessive, with notable infiltration by lymphocytes, plasma cells, and eosinophiles. One may control the infection; but resolution is slow and it takes a long time for the edema to be reduced to the point at which the flow of air to and from the middle ear proceeds normally. In some children the tube does not open regardless of treatment. These are the problem cases which require special management.

Manifestations

When acute serous otitis media becomes chronic it results in aggravated symptoms of deafness, tinnitus, sense of fullness and occasionally vertigo: symptoms which may persist for weeks and even months without pain.

The otoscopic picture is not difficult to discern. The drumhead is retracted. There may be a light pale yellowish tinge to the fluid as seen through the drumhead. The malleus in long-standing cases appears to be rotated, and the posterior handle of the malleus seems to stand out as a whitish chalk-like line. One may occasionally see the hairline of a fluid level, and if air enters the ear then small bubbles are visible through the drumhead, particularly during the act of swal-

lowing or yawning.

It must be remembered that a great many children with acute serous otitis media never come to the attention of the doctor at all. In these patients the acute inflammation of the nasopharynx and eustachian tube subsides, edema is reduced, air enters the ear, and drainage of the fluid takes place spontaneously through the tube. If the patient "burps" or blows his nose, air forcefully enters the middle ear. A "snap" in the ear is experienced and hearing suddenly returns. As has been said, it is with the patient with chronic or recurrent secretory otitis that the problem of management arises. As the negative pressure becomes more and more intense, a transudate accumulates in the middle ear from cells and capillaries of the middle ear mucosa.

"Glue Ear"

One form of chronic middle ear fluid that is commonly seen and has given rise to considerable discussion as to management is the mucoid or "glue ear." In this type of middle ear accumulation it is my firm belief that there has been inflammation of the middle ear mucosa, however mild. In these patients, however, the inflammation is frequently not sufficiently severe to require medical care. The middle ear becomes filled with a sticky tenacious mucous that gives a sense of fullness and increasing deafness. When this occurs the child is belatedly brought to the physician. The drum is dull, usually with some fullness around the periphery. The outline of the malleus may or may not be seen, and there is a definite lack of mobility of the drum when tested by positive and negative pressure. These are the difficult cases. A simple incision and aspiration may, in certain cases, if followed by politzerization of the eustachian tube, result in rapid improvement. Generally, however, the tube is still partially or completely obstructed and the secretions are too tenacious to drain through the eustachian tube. In those cases that fail to clear up after incision and withdrawal of the mucous by suction, a different management is required. These patients will require constant ventilation by means of a

teflon or polyethylene tube inserted through the drum into the middle ear and left in place until such time as the eustachian tube functions normally.

Severe Inflammatory Otitis Media

Another cause of "mucoid ear" is the oversight of the attending doctor in relation to management of a more severe inflammatory otitis media. Pain, fullness and deafness are present and the pain is severe enough to have the doctor called in attendance. He will usually give an antibiotic which may relieve the pain, but the fullness and deafness persists. The inflammation subsides with the antibiotic; but normal landmarks of the drum membrane are obscured and the middle ear fills with secretion. I am not describing the early stage of a severe acute otitis media where the drum is bulging and is intensely red, with continuous severe pain, fever, etc. This is a picture of acute otitis media that needs prompt incision and drainage. I am talking now of the acute middle ear that has subsided with antibiotics. These are the cases most commonly neglected. After such an acute otitis media every child or adult should have a follow-up examination for hearing loss.

Discussion

Acute Serous Otitis Media

Now let us discuss management in more detail — first, that of the acute serous otitis media or the noninflammatory type due to tubal obstruction at its orifice. This type of secretory otitis usually is greatly relieved by adenoidectomy.

In allergic children, even when the adenoid is not enlarged, infection increases the existing edema, which in turn obstructs the tube. This type of case can be treated conservatively in a child. The fluid in the middle ear does not require immediate aspiration. Shrinking solution can be supplied to the mucosa of the nose (Afrin, Neosynephrine, or any of the other preparations that are in common use). Antihistamines in combination with the shrinking agents can be quite effective. If the tube opens, the fluid will

drain and hearing will improve. If the serous otitis recurs and adenoid is present, a careful removal by direct visualization of the postnasal space and removal of all lymphoid tissue from the fossa of Rosenmueller and from the torus of the tube will generally cure the recurrent condition. This is done by elevating the soft palate so that the entire postnasal space is visualized. The main mass of adenoid is removed and then the remaining lymphoid tissue from the areas just mentioned with special punches. This includes the bands of lymphoid tissue that lie along the posterior pillar of the tonsil.

Tenacious secretions in the nose can be removed at home by using a large rubber bulb with an acorn shaped nasal tip placed in one nostril and closing off the other. When the infection subsides, gentle politizerization of the middle ear or auto-inflation can be performed. In other words, one should be patient with the acute serous effusions in children due to mechanical causes or mild infection of the postnasal space.

In recurring acute serous otitis or chronic serous otitis with or without exudate, something more drastic must be done if, after incision and aspiration, the transudate or exudate recurs. A ventilation tube should be inserted in the middle ear through the drum membrane and left there until such time as the acute or subacute inflammation in the nasopharynx subsides and normal aeration of the middle ear takes place.

Acute Suppurative Media

In the acute suppurative infections of the middle ear, the infecting organism should be determined by culture and the most effective antibiotic prescribed. This should be continued until there is complete resolution of the middle ear infection as indicated by return of landmarks and normal hearing.

It does not matter how skillfully one removes the adenoid, this tissue tends to regenerate in certain patients. This is particularly true in allergic children. Slight as this regeneration or hyperplasia may be, it is sometimes sufficient, when infected, to be the basis for recurrent obstruction of the

eustachian tube. In children with recurrent otitic problems, where I have personally performed the adenoidectomy, I am not at all reluctant to advise re-examination of the postnasal space under an anesthetic. I am no longer embarrassed by the necessity of removing a regrowth of lymphoid tissue. Secondary adenoidectomy is not an operation to be performed in a casual manner. The recurrent tissue must be trimmed flush with the basement membrane. Furthermore, allergic children must not be treated with indifferent allergic management, or serous otitic recurrence will be the rule.

Adhesive Otitis Media

Before concluding I must speak of a middle ear problem that is most serious: the so-called adhesive otitis media wherein adhesions bind the ossicles to each other or to the medial wall of the middle ear, a condition resulting from repeated infections of the middle ear. In my experience, I have yet to witness an adhesive otitis media following a true serous otitis media. Where there is no inflammatory ulceration there is no break in the epithelium, and where there is no break in the epithelium of the mucosa on the medial wall or the inner surface of the drum membrane, there will be no adhesions. Frequently, middle ear examination at the time of stapedectomy reveals bands of mucous membrane stretching across the chamber. These bands for the most part are normal. They are usually the result of the incomplete resolution of the myxomatous tissue present at birth before pneumatization of the middle ear chamber. These bands do not interfere with the mobility of the ossicular chain and they give rise to no symptoms whatsoever. The bands resulting from ulcerative inflammatory involvement of the middle ear mucosa, on the other hand, represent meaningful pathology. They may cause the malleus to be retracted against and adherent to the promontory. The head of the malleus and incus may similarly become fused. Placing a drainage tube in the middle ear will not alone be effective. The chamber must be forcibly aerated and the adhesive process disrupted.

Irradiation

A word about irradiation of the nasopharynx after adenoidectomy for recurrent growth is in order. For years I have used irradiation after removal of recurrent growth and felt that it was quite effective on lymphoid tissue. I am now somewhat reluctant to treat these young patients with small doses of x-ray because of the dangers that have been attributed to irradiation, even in relatively "safe" doses. I have never felt that the use of radium applicators in this area was wise.

Allergic Management

I close by re-emphasizing the need of good allergic management and thorough removal of lymphoid tissue in children as the prime treatment of tubotympanic dysfunction. When necessary the introduction of an indwelling microtube through the drumhead will provide continuous aeration of the middle ear chamber. In children to a degree, but particularly in adults, persistent serous otitis media should alert the clinician to the possibility of nasopharyngeal malignancy.

Medical Pomposity

With erudite profundity,
And subtle cogitabundity,
The medical expert testifies in court;
Explains with ponderosity,
And keen profound verbosity
The intricate nature of the plaintiff's tort.

Discoursing on pathology,
Anatomy, biology,
Opines the patient's orbit suffered thus:
Contusions of integuments
With ecchymose embellishments,
And bloody extravasation forming pus.

A state of tumerosity
Producing lachrymosity,
Abrasion of the cuticle severe,
All diagnosed externally,
Although he feared, internally
Sclerotic inflammation might appear.

The jury sits confused, amazed,
By all this pleonasm dazed,
Unable to conceive a single word,
All awed, they think with bated breaths
The plaintiff died a thousand deaths —
What agony and pain he had endured!

But then the counsel for defense,
Devoid of garrulous eloquence,
Asked, "Isn't it true that all you testified
Means merely from a punch or two
The plaintiff's eye was black and blue?"
"Yes, that's correct," the doctor meekly sighed.

— F. William Saul, M.D.: *Pink Pills for Pale People*.



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BLUE SHIELD
OF MINNESOTA



Tympanoplasty for Chronic Otitis Media

FREDERICK R. GUILFORD, M.D.*
Houston, Texas

IN SPITE of antibiotics, chronic ear suppuration following acute otitis media or trauma, or in association with cholesteatoma, remains a common clinical finding in the practice of otolaryngology. A high incidence of this condition will be found in general medical practice, provided a careful examination is done with a magnifying otoscope.

Physical Findings

Intermittent or persistent purulent discharge may be present especially following bathing, swimming, or upper respiratory infection and hearing loss in the involved ear. On otoscopic examination relatively large areas of the tympanic membrane may be absent without causing significant hearing impairment, but the loss of ossicular continuity, which may be a late sequela, usually results in hearing loss.

Indications for Surgery

While it would appear that antibiotics could control all types of infection, it is now apparent that these drugs alone are inefficient in controlling chronic suppuration of the middle ear and mastoid. Effective treatment of the condition often requires tympanoplasty or surgical removal of the suppurative processes and repair of the ossicular chain and tympanic membrane. The aims of tympanoplasty are control of the suppurative process and reconstruction of the damaged conduction mechanism; the ossicular chain and tympanic membrane.

Control of Suppuration

Conservative measures such as frequent aspiration of the middle ear followed by irrigation with appropriate antibiotic solution will often control the suppurative process prior to surgical reconstruction; however, direct surgical measures, such as mastoidectomy, removal of granulations from the middle ear, or curettage of the hypotympanic cells may

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be necessary as the initial step in the reconstructive process. The use of the binocular operating microscope aids materially in this surgery. Conservation of tissue commensurate with accepted surgical principles is the rule in order to restore as near normal functional anatomy as possible. The external auditory canal is either left intact or reconstructed in order to avoid a postoperative

mastoid cavity. The reconstructed tympanic membrane, then, is a barrier to suppuration as in the normal condition since its presence protects the middle ear from contamination.

Repair or Reconstruction of the Ossicular Chain

Repeated infections of the middle ear, as may occur with perforation of the tympanic membrane, may result in disruption of the ossicular chain. The disruption is usually due to necrosis of the long process of the incus and results in dissolution of the incudostapedial articulation. The disruption may also affect the manubrium of the malleus and occasionally the arch of the stapes (Figure 1). When a cholesteatoma is present, erosion of the ossicles and adjacent osseous tissue in the temporal bone may occur. A persistently perforated ear drum may be complicated by invasion of squamous epithelium into the middle ear and mastoid and development of this destructive process. Generally, this complication is more frequently found in perforations located in the peripheral areas of the tympanic membrane. A cholesteatoma may cause other serious complications, such as intracranial lesions, but these are rare.

The control and removal of cholesteatoma and other irreversibly diseased processes of chronic suppuration is the prime objective of temporal bone surgery. In the last decade techniques of reconstruction of the tympanic membrane, ossicular chain and posterior wall of the ear canal (in order to avoid a mastoid cavity) have been developed. Radical removal of irreversibly diseased tissue but retention of functional structures is the rule. In addition, recent results suggest that homograft ossicles (especially the incus may be used to replace diseased ossicles or those which have been destroyed.

Satisfactory results are not obtained following the use of plastic materials to reconstitute the ossicular chain, and it may be necessary to reposition the incus or malleus in order to form an intact conduction mechanism between the tympanic membrane and mobile stapes to afford good hearing results (Figure 2). When a member of the chain is

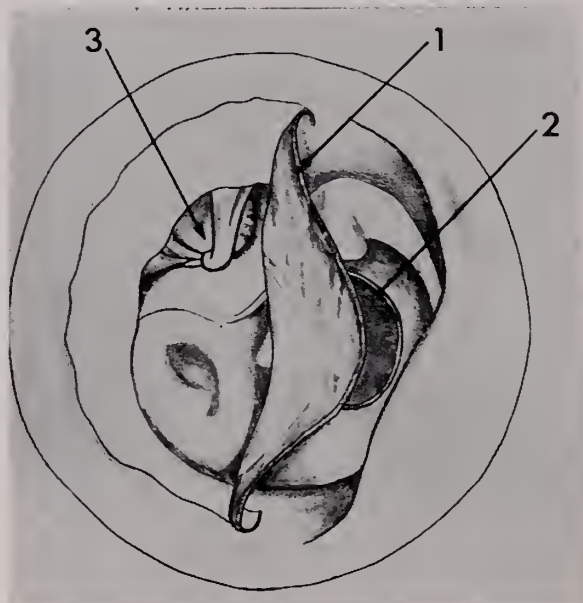


Fig. 1-a reveals the meatal flap and posterior one-half of the tympanic membrane elevated (1), large central perforation (2), and intact incudostapedial joint (3).

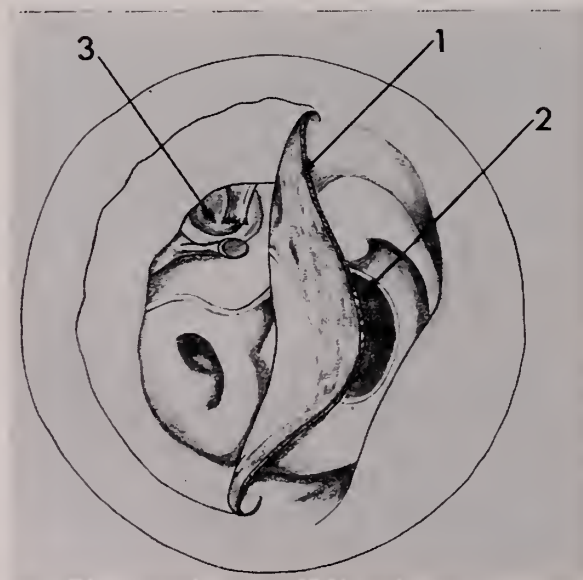


Fig. 1-b, the elevated meatal flap and posterior one-half of the tympanic membrane (1), perforation (2), and disrupted incudostapedial joint (3) are shown.

irreversibly destroyed, it can be replaced by cortical bone fashioned from an adjacent area of the skull or more recently by the homograft ossicle which is preserved by freezing. Wire can also be used successfully to bridge small gaps in the ossicular chain, especially between the malleus and the stapes.

Repair of the Tympanic Membrane

Partial or total defects of the tympanic membrane may be reconstructed providing the suppuration and related processes have been successfully controlled. The operation is usually performed as a one stage procedure,

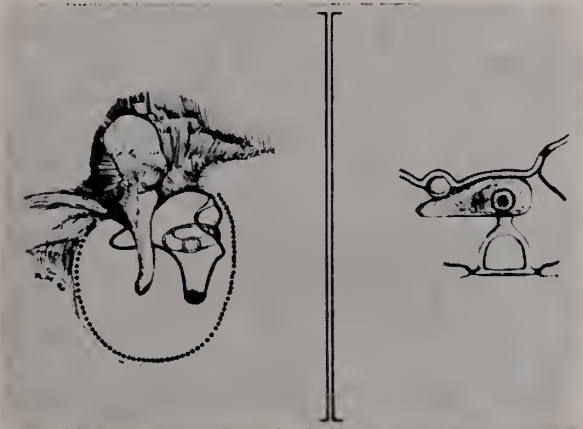


Fig. 2 — An example of reconstruction of the ossicular chain by repositioning of the incus shown in lateral and cross-sectional views (previously published in the *Laryngoscope* 75:236, February 1965).



Fig. 3-a illustrates the large kidney shaped perforation in the tympanic membrane and a portion of the adjacent wall of the external auditory canal.

but occasionally the reconstructive portion of the operation is performed later.

Early efforts to use the skin from the post-auricular area or extremities for repair of the tympanic defect were not completely successful because of a tendency for complications, such as the occurrence of epidermoid cyst and dermatitis of the graft in relation with the skin appendages. The skin of the ear canal has proven to be more adaptable when combined with a thin layer of fibrous tem-



Fig. 3-b shows the incisions for removal of the skin from the medial portion of the external auditory canal and tympanic remnant.



Fig. 3-c, the skin has been removed medial to the incisions in continuity with the skin on the tympanic remnant.



Fig. 3-d, an appropriate sized piece of temporal fascia has been replaced on the tympanic remnant covering the perforation.

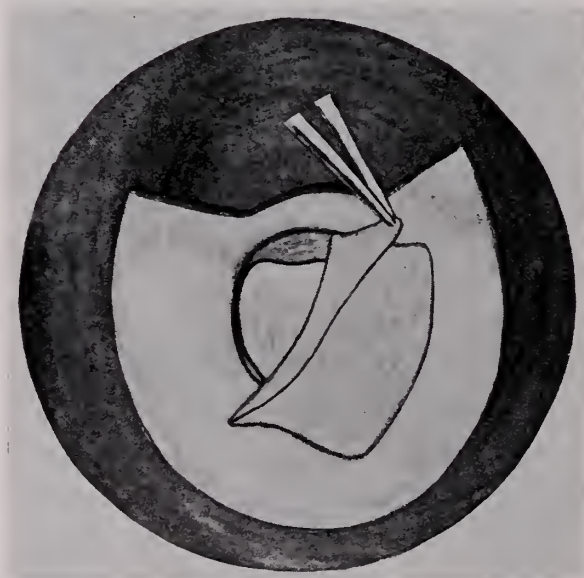


Fig. 3-e illustrates the placing of the skin from the external auditory canal over the fascia and adjacent canal.

poral fascia tissue. With this combination of tissues, it is possible to afford reconstruction of the three layers normally present in the tympanic membrane (Figure 3).

The skin of the lateral surface of the tympanic remnant and medial part of the external canal is elevated as a flap, or completely removed, and the middle ear carefully inspected for invading squamous epithelium or other pathologic processes. A thin layer of temporal fascia is obtained through existing or separate incisions. The fascia is tailored to fit the area precisely and is then placed over the perforation and the denuded surface of the tympanic remnant or overlapping onto the adjacent denuded external auditory canal. The skin of the external canal is then replaced in such a fashion that it overlaps the layer of the fascia. The squamous epithelium then migrates during the healing period across the lateral surface of the fascial graft, and the continuity of the tympanic membrane is again intact. The undersurface of the fascial graft is covered by the migrating mucous membrane from the middle ear, and the three layers of the tympanic membrane, namely the mucous membrane, the fibrous layer, and the external skin, are restored.

Conclusions

It is evident that tympanoplastic surgery affords the possibility of hearing restoration as well as control of infection in the presence of the persistent perforation of the tympanic membrane due to traumatic or chronic suppurative processes. The application of these reconstructive measures in temporal bone surgery is a significant advance in otolaryngology, in the tradition of the remarkable development of surgical rehabilitation in modern medical practice.

Bedridden Truth

It is the most useful prerogative of genius to rescue truths from the neglect caused by the very circumstance of their universal admission. Truths, of all others the most awful and interesting, are too often considered as so true that they lose the power of truth, and lie bedridden in the dormitory of the soul. — Samuel Coleridge

Partial Laryngectomy

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PARTIAL LARYNGECTOMY refers to the broad term covering hemilaryngectomy for cancer of the true cord; subtotal supraglottic laryngectomy for cancer of the epiglottis, and partial laryngopharyngectomy for cancer of the pyriform fossa or base of tongue.

Malignant tumors arising in these areas behave differently from one another with reference to structures invaded, aggressiveness, and prognosis. All of these partial laryngectomy operations are covered under the term "conservation surgery."

This paper will deal with the surgical results to date by comparing cancers in four primary locations: one of the cord treated by irradiation and hemilaryngectomy and three managed by supraglottic laryngectomy or subtotal pharyngolaryngectomy. The cases have been followed for two to eleven years. The absolute survival rate includes only those patients living and free of tumor. The survival rate includes both those patients free of disease and those who died of intercurrent disease. Any patient who expired within two months of surgery was included in the death of disease group.

Cancer of the Larynx

Cancer of the larynx is divided into four groups:

Cancer of the glottis refers to neoplasms restricted to the true membranous cord, vocal process on one or both sides. The floor of the ventricle is included in the glottic group and for a distance of one centimeter below the medial border of the cord, where the intrinsic muscles end.

Cancer of the subglottis refers to primary lesions immediately beneath the vocal cord in the anterior or lateral portions down to the lower border of the cricoid cartilage.

Cancer of the epiglottis, or supraglottis,

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belongs with the larynx group and is restricted to the laryngeal surface of the epiglottis and the false cords or ventricular band.

Transglottis cancer refers to lesions crossing the ventricle.

Carcinomata of the Laryngopharynx

Carcinomata of the laryngopharynx are divided into two groups on the basis of anatomical location, biologic behavior, incidence of cervical metastases and eventual prognosis. Because of the characteristics indigentous to each of the following groups, surgical therapy must be altered accordingly.

Superior hypopharyngeal carcinoma includes lesions of the lingual surface of the epiglottis, the valleculae and the base of the tongue.

Inferior hypopharyngeal carcinoma includes lesions of the pyriform fossa, aryepiglottic folds and posterior pharyngeal wall.

Cervical Node Metastases

Cancer of the true cord metastasizes infrequently to the neck, whereas cancer of the epiglottis metastasizes more frequently. Carcinomata of the laryngopharynx are associated with a high rate of metastases to cervical lymph nodes.

Radiotherapy has been shown to yield poor results in controlling cervical metastases.^{4,7} Therefore it is mandatory that surgical treatment of carcinoma of laryngopharynx be based on a knowledge of the probable incidence of metastases and include a method of controlling them. It is now generally accepted that radical neck dissection in continuity with resection of the primary tumor is the procedure of choice when the presence of cervical metastases is probable.^{10,12,14}

Every patient with palpable cervical lymph nodes associated with a lesion in the laryngopharynx should have radical neck dissection performed at the time of resection of the primary tumor. A question arises as to what to do in the absence of cervical adenopathy. The incidence of occult metastases associated with supraglottic carcinoma is 10% and does not justify the performance of elective neck

dissection. However, an incidence of 40% occult metastases from carcinomata of the inferior and superior hypopharynx is high enough to justify elective radical neck dissection. It is well recognized that waiting for the appearance of metastases and performing staged surgery result in a higher incidence of local recurrences.¹⁰ Patients with occult metastases with elective neck dissections have an increased survival over patients who have had therapeutic neck dissection.^{9,12,14}

Bilateral cervical lymph node metastases have occurred infrequently in our patients with occult cervical metastases on the side of the lesion. They are, however, fairly common in patients with clinical metastases on the side of the lesion. In almost all cases contralateral metastases are clinically present when the patient is first seen. Of five patients who had staged neck dissections for cervical metastases from inferior hypopharyngeal carcinoma all have died of disease within twelve months, whereas four of six patients who had one-stage bilateral neck dissection with resection of a hypopharyngeal tumor are alive and well two or more years postoperatively. We therefore advocate one-stage bilateral neck dissection with resection of the primary lesion when bilateral cervical adenopathy exists.

Treatment of the Primary Lesion

Radiotherapy has yielded good results for cancer of the true cord when the tumors were small and restricted to the membranous portion. On the other hand, irradiation failures were noted when the lesion crossed the anterior commissure, extended into the subglottis more than 5 mm., and involved the vocal process. These more extensive cordal lesions should be treated by hemilaryngectomy.

Radiotherapy has yielded uniformly poor cure rates in the treatment of laryngopharyngeal lesions regardless of the site of the lesions. Radiation cure rates of 20 to 25% for supraglottic carcinoma and smaller figures for hypopharyngeal carcinoma have recently been reported.^{2,3,5}

The argument that laryngectomy can al-

ways be performed should radiotherapy fail is fallacious. In this instance one must deal with the complications of irradiation-induced tissue changes as well as with an altered resistant tumor cell population which often extends far beneath apparently normal mucosa. As a result, secondary surgery does not yield as good cure rates as primary surgery. There is, however, some evidence that planned preoperative radiotherapy followed immediately by surgical resection may have merit.^{8,15,16}

Surgical therapy for carcinoma of the laryngopharynx has, in the past, consisted almost entirely of widefield total laryngectomy or total laryngopharyngectomy. Since involvement of the glottis is a late development in this type of cancer, total removal of the larynx seems an unnecessarily radical procedure. It has been our experience that as many as 50% of lesions of the laryngopharynx may be removed with their lymphatic drainage tracts by *subtotal* laryngeal and pharyngeal resection and radical neck dissection.

Involvement of the pre-epiglottic space by laryngopharynx cancer is very common and is the most frequent cause of failure in too conservative surgical resection. It is imperative that the hyoid bone and pre-epiglottic space be removed in every case. This is accomplished by both total laryngectomy¹⁰ and subtotal laryngectomy.¹³

Subtotal laryngectomy avoids the stigma too of loss of phonation and permanent tracheostomy and in our hands has given as good or better cure rates than total laryngectomy.

The success of subtotal laryngectomy is dependent upon careful patient selection. The procedure is not suitable for very large

extensive lesions. The preoperative laryngograms and laryngoscopy are essential. Cartilage destruction and extensive glottic involvement with cord fixation are contraindications to this operation.

The technical factors important in the surgical resection and the rehabilitation of deglutition have previously been reported.^{12,13,17,19}

Results of Treatment of Cancer of the Glottis Treated by Irradiation and Hemilaryngectomy

A series of 50 cases of glottic carcinoma treated by irradiation alone has yielded an overall absolute five-year cure rate of 78% and a tumor survival rate of 92%.¹⁸

It must be understood that these cases were first screened for suitability. Small lesions of the membranous cord were predominant. Failures were principally large glottic tumors involving the vocal process, subglottis or anterior commissure.

We have performed seventeen hemilaryngectomies after irradiation failed, with an absolute two-year salvage rate of 65%. Two more patients were salvaged by total laryngectomy and four died of intercurrent disease. This means that only one of the 17 has died of his cancer (Table 1-A) since this data was compiled.

TABLE 1-A
Survival Rate of Hemilaryngectomy after Radiation Therapy Failure

	2 years	5 years
Living and well	11	2
Living with disease	1	0
Death without disease	4	3
Death with disease	1	0
Absolute survival	11/17 (65%)	2/5 (40%)
Tumor survival	15/17 (88%)	5/5 (100%)

TABLE 1-B
Survival Rate of Hemilaryngectomy

	2 years	5 years
Living and well	46	16
Living with disease	0	0
Death without disease	7	0
Death with disease	7	6
Absolute survival	46/60 (77%)	16/22 (73%)
Tumor survival	53/60 (88%)	16/22 (73%)

The results of 60 hemilaryngectomies, in previously untreated patients, yielded an absolute two-year survival rate of 77% and a tumor survival rate of 88% (Table 1-B). See Table 2 for an outline of the failures. The results of laryngofissures at this institution are not included.

Results of Treatment of Carcinoma of the Larynx or Laryngopharynx by Total Laryngectomy and Subtotal Laryngectomy

Supraglottic Carcinoma

A series of 39 consecutive supraglottic carcinomata treated by widefield total laryngectomy and radical neck dissection at our institution were recently reported.¹ The tumor survival rate at five years was 80%.

Since 1958 we have performed a subtotal supraglottic laryngectomy on supraglottic carcinoma whenever possible. The results of this type of surgery are shown in Table 3 and they are seen to be comparable to those obtained by total laryngectomy.

TABLE 2
Analysis of Failures (Hemilaryngectomy)

Cause of Failure	1	2	3	4	5	6	Total
Death with Disease	Follow-up in Years						
Local recurrence	1			1			2
Node metastases							0
Operation death	2						2
Recent PE negative Cause of death?	1	1		1			3
Death without Disease							
Second primary	1	1					2
Myocardial infarction	2			1			3
Congestive heart failure	1						1
Dissecting aneurysm		1					1
							14

The most important point in the analysis of the failures in this group is that only five patients of 65 have had recurrence of their cancer. The tumor survival rate was 77%. Three patients had cervical node metastases with persistent disease in the lateral neck; one patient had late distant metastases, and none developed a recurrence at the site of the larynx. It has been our experience that patients dying of persistent carcinoma of the laryngopharynx will manifest evidence of persistence within twelve months of the primary surgical procedure in over 90% of the cases.

Supraglottic subtotal laryngectomy is a valid cancer-excising surgical procedure which carries small risk of local persistence of disease if carefully done on selected patients. At the same time normal phonatory mechanisms are retained without loss of normal deglutition (Table 4).

Carcinoma of Inferior Hypopharynx

In a series of 59 consecutive patients with carcinoma of the inferior hypopharynx treated by total laryngectomy and radical neck dissection, the absolute five-year survival rate was 30%. Of the 28 failures, 16 patients died of persistent disease. Eight developed recrudescence in the operated side of the neck, and six developed recrudescence in the pharynx, with two patients dying of distant metastases. Fifteen of 16 patients dying of disease manifested recrudescence within twelve months and were dead in eighteen months.

A large number of inferior hypopharyngeal carcinomata involving the pyriform fossa and the posterior pharyngeal wall are of such a size that the endolarynx and glottis are free of disease; these lesions have

TABLE 3
Survival Rate of Supraglottic Carcinomas Treated by Horizontal Subtotal Laryngectomy

	2 years	5 years
Living and well	43	9
Living with disease	2	1
Death without disease	9	4
Death with disease	10	3
Absolute survival	43/64 (67%)	9/17 (53%)
Tumor survival	52/64 (81%)	13/17 (77%)

been resected by subtotal laryngopharyngectomy and radical neck dissection. The results are shown in Tables 5 and 6.

An equivalent result is obtained by subtotal resection in this group of 29% absolute survival rate. The fact that the results approximate those obtained by total sacrifice of the larynx supports the use of conservation techniques.

There were eight patients who had recurrence of their carcinoma. There were five cervical recurrences and two primary recurrences, and one patient developed pulmonary metastases. Only one of these recurrences developed later than eighteen months postoperatively. This developed four years postoperatively in a patient who had multiple oropharyngeal carcinomas, and it may have represented another primary lesion.

Superior Hypopharynx

Until the present time most lesions in this area have been treated almost solely by irradiation. The results have been generally poor and have approximated 20% or less.²

We feel that involvement of the pre-epiglottic space as well as cervical lymph node metastases are factors in irradiation failure.

Therefore since 1958 we have performed an extended supraglottic subtotal laryngectomy on these cases with the results depicted in Tables 7 and 8.

In the group of failures 15 of 19 patients have died of persistent disease, nine with persistence in the head and neck. Six had disseminated metastases. In this group all the patients dying of persistence were dead

TABLE 4
Analysis of Supraglottic Failures

Cause of Failure	1	2	3	4	5	6	7	8	Total
Death with Disease									
Time of Death or Current Follow-up in Years									
Cervical recurrence	1								1
Primary recurrence									0
Contralateral neck recurrence									0
Disseminated metastasis	1								1
Operation death	4								4
Pneumonitis	2								2
Inadequate information	2								2
Living with Disease									
Cervical recurrence						1			1
Contralateral neck metastasis		1							1
Death without Disease									
Second primary	1			2					3
ASHD		1		1	1				3
Auto accident	1								1
Pneumonitis	1								1
Emphysema	1								1
									21

TABLE 5
Survival Rate of Inferior Hypopharynx Carcinomas Treated by
Horizontal Subtotal Laryngectomy

	2 years	5 years
Living and well	12	4
Living with disease	0	0
Death without disease	8	7
Death with disease	10	3
Absolute survival	12/30 (40%)	4/14 (29%)
Tumor survival	20/30 (67%)	11/14 (78%)

within eighteen months.

The two-year survival rate is therefore a valuable figure as to the number of patients likely to develop persistent hypopharyngeal disease.

In the hypopharyngeal groups there was a combined survival rate of 40% of 62 patients in a disease which previously carried a high mortality.

Combined Therapy

The objective of combined therapy, preoperative irradiation followed by surgery, is to improve survivals and cure rates. Naturally, where the cure rates are very high the demonstration of the value of irradiation would be difficult. Thus preoperative irradiation is not indicated for any glottic lesion where surgery is contemplated. The value of preoperative irradiation for epiglottic carcinomas is questioned. There are exceptions, however: a very large supraglottic cancer encroaching upon pharyngeal structures of the larynx, (aryepiglottic fold and aryte-

noid) or the presence of palpable adenopathy.

The cause of failure of surgery for hypopharyngeal carcinoma is often due to persistent disease. Because of the relatively high risk of recrudescence we have elected to treat patients with this disease with preoperative doses of irradiation followed by immediate surgery. By this mode of therapy we hope to reduce the incidence of implantation and metastases produced at the time of surgery.

The dose of irradiation is 2000-3000 rads over two to three weeks. We have chosen this dose in an effort to avoid an increase in surgical complications and still obtain an effective morbidity of the majority of tumor cells.

This series is too recent to discuss cure rates; however, analysis of the failures is valuable. As noted in a series involving patients treated by surgery alone, recrudescent disease has uniformly been manifest within the first twelve months of risk. Thus far we

TABLE 6
Analysis of Inferior Hypopharynx Failures

Reason for Failure	1	2	3	4	5	6	7	Total
Time of Death in Postoperative Years								
Death with Disease								
Cervical recurrence	3	1						4
Primary recurrence		1		1				2
Contralateral neck recurrence			1					1
Pulmonary metastasis	1							1
Inadequate information	2							2
Death without Disease								
Second primary	1	1				1		3
Pneumonia			1	1				2
Myocardial infarction		1		1				2
Inanition		1						1
								18

TABLE 7
Survival Rate of Superior Hypopharynx Carcinomas Treated by
Horizontal Subtotal Laryngectomy

	2 years	5 years
Living and well	13	4
Living with disease	0	0
Death without disease	0	0
Death with disease	19	6
Absolute survival	13/32 (41%)	4/10 (40%)
Tumor survival	13/32 (41%)	4/10 (40%)

have preoperatively irradiated 60 patients with inferior hypopharyngeal carcinoma and 19 patients with superior hypopharyngeal carcinoma. These patients have all had the surgical procedure performed which was indicated prior to any irradiation. In the inferior hypopharyngeal group only 12 of 60 (20%) patients have developed persistence in the first twelve months compared with 24 of 73 (33%) in the non-irradiated group. Of the 19 patients with superior hypopharyngeal carcinoma, three of 19 (16%) have developed persistence in the first twelve months compared with nine of 23 (40%) in the non-irradiated group.

Tentatively it appears that planned preoperative irradiation and immediate surgery will be a valuable adjunct in the treatment of carcinomata of the laryngopharynx in which there is a relatively high risk of recrudescence.

Summary

Surgical therapy for carcinomata of the larynx and laryngopharynx has produced encouraging results. Early glottic cancer, that is, a small cancer of the membranous cord can be cured by full irradiation. Larger lesions involving the anterior commissure

and vocal process or extending subglottically for 5 mm. should have a hemilaryngectomy. Total laryngectomy is not indicated in these lesions.

Subtotal surgical therapy of carcinoma of the laryngopharynx and supraglottis has produced encouraging results. These may be improved further by planning preoperative irradiation and surgery. Surgical treatment of this disease does not always entail total laryngectomy as was previously the situation. As many as 50% of patients seen in our office with this disease were treated by larynx-conserving operations with the gratifying result of cancer cure and preservation of normal phonation and deglutition.

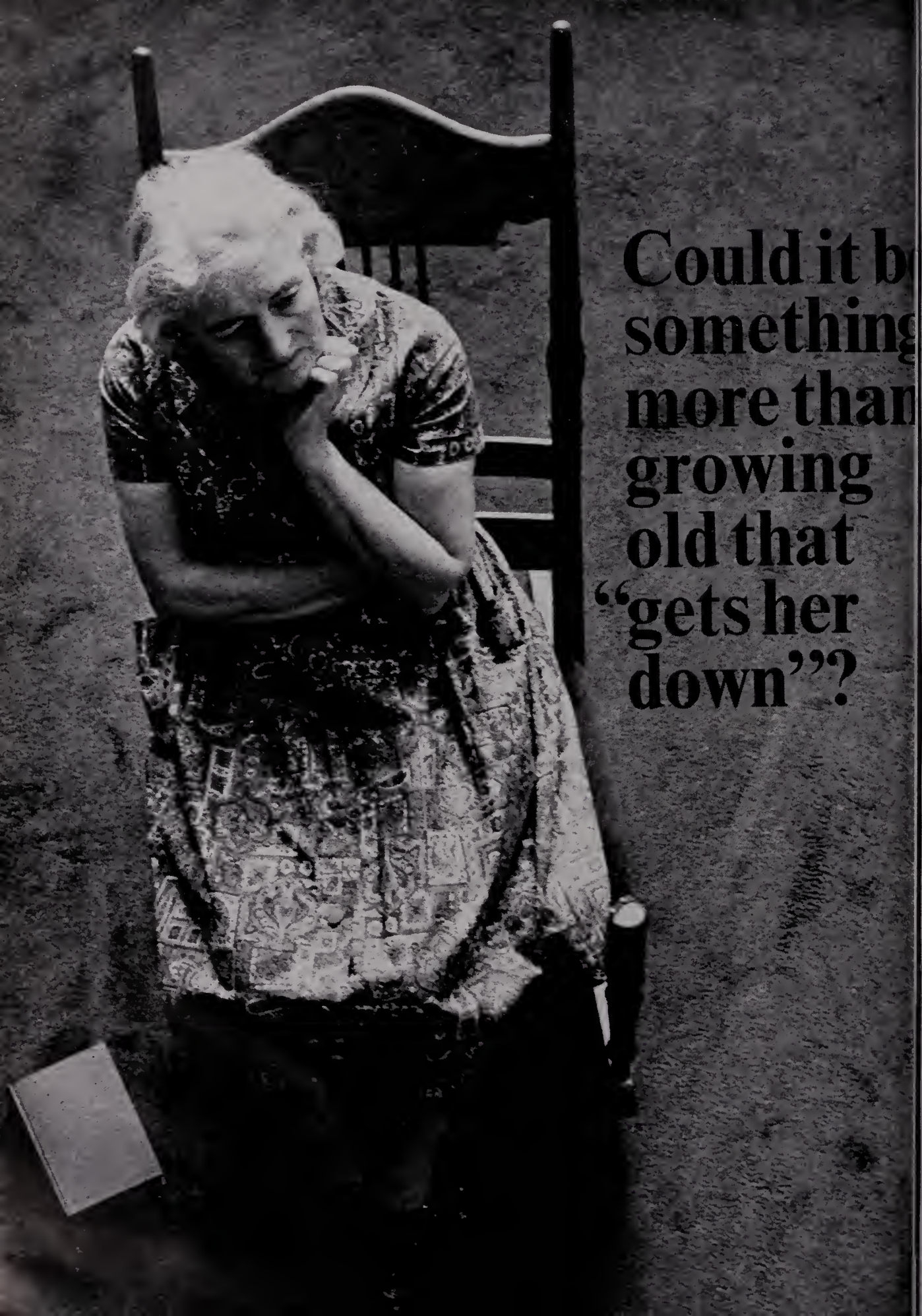
TABLE 8
Analysis of Superior Hypopharynx Failures

Cause of Failure	1	2	3	4	5	Total
Death with Disease	Time of Death in Postoperative Years					
Cervical recurrence	1	2				3
Primary recurrence	2	3				5
Disseminated metastasis	1	5				6
Contralateral neck recurrence		1				1
Operation death	2					2
Pneumonitis	1					1
Inadequate information	1					1
						19

References

1. Bauer, W. C., McGavran, M. H. and Ogura, J. H.: An Analysis of 39 Cases of Supraglottic Carcinoma of the Larynx Treated by Total Laryngectomy and Radical Neck Dissection. Presented at the Society of Rhinology, Otolaryngology, and Laryngology, Hollywood Beach, Florida, 1962.
2. Daley, V. M.: The Place of Radiotherapy in the Treatment of Tumors of the Base of the Tongue. *Amer J Roentgen* 93:20, 1965.
3. Garland, H.: The Current Status of Radiotherapy in Carcinoma Laryngis. *Ann Otol* 73:488, 1964.
4. Jacobsson, F.: Carcinoma of the Hypopharynx. *Acta Radiol* 35, 1, 1951.
5. Lederman, M.: Role of Irradiation in Treatment of Cancer of the Hypopharynx Post Cricoid and Cervical Esophagus. Paper given at International Workshop on Cancer of the Head and Neck, New York, May, 1965.
6. Leroux-Robert, J.: Diagnostic et Indications des Cancers du Sinus Piriforme. *Rev Prat* 6:2637, 1956.
7. Martin, H.: The Treatment of Metastatic Cervical Carcinoma. *Ann Surg* 114:972, 1951.
8. McGavran, M. H., Ogura, Joseph H., Powers, W. E.: Small Dose Preoperative Radiation Therapy. *Radiology* 83:509, 1964.
9. McGavran, M. H., Bauer, W. C., Ogura, J. H.: Carcinoma of the Pyriform Sinus. *Arch Otolaryng* 78:826, 1963.
10. Ogura, J. H.: Surgical Pathology of Cancer of the Larynx. *Laryngoscope* 65:867, 1955.
11. Ogura, J. H. and Bello, J.: Laryngectomy and Radical Neck Dissection for Carcinoma of the Larynx. *Laryngoscope* 62:1, 1952.
12. Ogura, J. H.: Laryngectomy and Lateral Pharyngotomy. W. F. Prior, *Otolaryngology Vol V*.
13. Ogura, J. H. and Mallen, R. W.: Carcinoma of the Epiglottis and Hypopharynx: Conservation Surgery of the Larynx. Presented at the International Workshop on Head and Neck Cancer, New York, May, 1965.
14. O'Keefe, J. J.: Concerning the Criteria of Operability in Laryngeal Cancer. *Ann Otol* 68:453, 1951.
- 15-19. May be secured from the author or the reprints.

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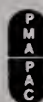
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The Injured Larynx

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SPEED AND MORE speed is the essence of both the causation and the management of injuries to the larynx. Faster and faster automobiles, higher speed limits, more high-speed freeways result in more and more anterior neck injuries by striking steering wheels and dashboards. Speed and increased efficiency in rendering emergency care either at the site of an accident or at a close-by hospital also result in more laryngeal trauma being brought to the laryngologist. And some speed is needed in the successful care of these patients.

Restoration of the normal functions of the larynx after injury will be the most complete and take the shortest time if the patient is seen immediately by the laryngologist. Many times a tracheotomy has already been performed either at the site of the injury or with the patient's first medical care. This does not change the dictum that the laryngologist should start his treatment immediately unless there is an exceptional reason for delay.

It is important to determine two things in the patient whose anterior neck has been struck by the steering wheel, the dashboard, or other objects such as a fist, a cable, a stick, a knife, or a bullet. These two are: first, has the airway been compromised or obstructed; second, has there been a tear in the lining of either the air passages or the food passages?

Diagnosis

External examination of the neck, indirect mirror examination, X-ray examination, direct laryngoscopy, tracheoscopy, and upper esophagoscopy in that order are needed to make a diagnosis and determine management.

Subcutaneous Emphysema

First, one should look and feel for subcutaneous air or crepitus.

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Generalized crepitus of the neck usually means a rather large tear of the trachea or possibly lower parts of the respiratory system. Localized or only spot emphysema usually means a small tear or may denote a rupture of just a ventricle. A tear of one false cord has resulted in air over one wing of the thyroid cartilage, and tears of the hypopharynx have produced subcutaneous air in small lateral neck areas. Tears of the larynx tend to give small areas of subcutaneous emphysema, while tears of the trachea seem to result in more wide-spread emphysema.

The Larynx

Loss of the thyroid notch or the prominence of the "Adam's apple" in the male usually means that the laryngeal cartilages have been fractured and/or displaced posteriorly. If it cannot be seen or felt in the female the same possibility is indicated. Sometimes actual mobility, displacement, crepitus of fractured cartilage, dislocation, and point tenderness can be palpated.

Dyspnea, stridor, cough, voice changes, and expectoration of bloody, frothy mucus should be looked for. The patient must be questioned about difficult or painful swallowing. This latter usually means a tear of the hypopharynx.

Laryngoscopy

Indirect examination with the laryngeal mirror comes next. Pooling of saliva with or without fresh blood usually means a posterior hypopharyngeal tear. However, a vertical tear of the posterior surface of the cricoid eminence has also had the same result. Pooling of saliva without blood could mean a tear of the cricopharyngeal area or its immediate sub-area. Foreshortening of the anteroposterior diameter of the glottis means dislocation of one or both arytenoids from the cricoid cartilage. Usually there may be swelling and sometimes hematoma of the arytenoids or false cords, paralysis or restriction of the movements of the larynx, or dislocations of the structures of the larynx; or an arytenoid may be tilted medially as well as posteriorly, concealing the

true cords and glottis. Recently a tilting inwards of the entire supra-glottic structures of one side, that is the aryepiglottic fold, the false cord, and the arytenoid, was most prominent.

X-ray Examination

Lateral X rays of the neck should be obtained in order to identify the presence of air in the soft tissue spaces. Air in the retropharyngeal or precervical vertebral area usually means a tear of the hypopharynx, pyriform sinus, cricopharyngeus or uppermost esophagus. Air resulting from tracheal or laryngeal tears is more widespread and is anteriorly, laterally or posteriorly placed. Air in the root of the neck, mediastinum or pleural cavities usually denotes tracheal or lower tears. Good X rays may also demonstrate airway or structural deviation of the larynx.

Direct Laryngoscopy

The first direct laryngoscopy should always be done with basal and topical anesthesia so that the presence or absence of laryngeal paralysis can be noted. A second direct examination can be done with general anesthesia if necessary. The laryngoscope proves or adds to the laryngeal mirror examination. Often in injuries, the epiglottis must be elevated to reveal the trauma to glottic structures. Tears of the pyriform sinuses and cricoid area are often seen only when the larynx is lifted forwards.

Equally important and necessary is the passage of the largest bronchoscope. This will be therapeutic as well as diagnostic. Tears of the sub-glottic area and the trachea all the way to the carina should be searched for. Small tears will probably be treated conservatively, but large tears, sometimes completely circumferential, may mean separation of one tracheal ring from another or the separation of the first tracheal ring from the cricoid. These latter will necessitate open surgery and suturing of the torn parts. Again, it must be stressed that any air in the neck calls for complete examination of the entire trachea by means of the bronchoscope. Not only is the passage of the

bronchoscope diagnostic, but it also constitutes the first, the most important, and sometimes the only treatment that is needed. The bronchoscope is used to reduce, elevate, or "iron out" the fractured and dislocated parts of the laryngeal cartilages. Sometimes the immediate improvement following this procedure can be seen with the withdrawal of the scope which has lengthened the anteroposterior diameter of the larynx and produced a more normal topography of the parts. Sometimes, as in the recent instance of the tilting inwards of all of one side of the larynx, a second "ironing out" under general anesthesia has resulted in very adequate restoration of the airway.

Finally, an upper esophagoscope should be used to inspect the posterior wall of the oropharynx, the hypopharynx, the pyriform sinuses, the postcricoid area, the cricopharyngeal area and the upper half of the esophagus.

Treatment

"Ironing Out" the Trachea

Many times the initial "ironing out" is all that is needed in treatment; and often following it the tracheotomy tube that may have been used in the emergency can be removed in a few days. One should usually wait a week and then determine on the basis of repeated indirect mirror examinations whether subsequent "ironing out" with the bronchoscope, or possibly with the passage of rigid metal laryngeal dilators, is needed.

Indwelling Plastic Tube

If these repeated dilations do not result in a good airway, it is then advisable to place an indwelling section of plastic tubing for continuous dilation and reduction of dislocation until subsequent healing results in an adequate airway. A section of a size 9 or 10 Portex tube or endotracheal tube is ideal.

These have the rigidity needed and do not seem to result in any irritation or infection of soft tissues while being dilated and held in place. These sections are introduced into the trachea through the tracheotomy opening and their lower bevelled end is tied to the especially fenestrated and ringed silver

tracheotomy tubes. Such sections are usually left in place a minimum of three or four weeks and can be replaced as well as removed through the tracheotomy opening in gradually increasing sizes if necessary.

Open Operation

If the initial examination reveals a large or circumferential tear of the trachea, or if separation between tracheal rings or from the cricoid cartilage is demonstrated, an open operation must be done. At this time all torn areas are sutured, an indwelling section should always be placed, and the specially fenestrated and ringed tracheotomy tube should be used.

Nasogastric Feeding Tube

If this first examination demonstrated a tear of the hypopharynx, a nasal feeding tube should be placed and left in place for all feedings for usually one week. In one patient a tiny tear of the posterior wall of the uppermost esophagus was also successfully treated with just an indwelling nasal feeding tube. But larger and lower esophageal tears have had to be repaired by an external surgical approach.

For the ideal management the above treatment is that which should be instituted when the patient is seen in the first few hours or days after his injury. Of course, an exception would be that patient who has other injuries to the skull or brain, or other fractures which preclude direct examination and treatment. Mediastinal and pleural air might be another contraindication, as would other internal injuries that would make such a procedure hazardous. The above method of treatment presupposes a closed injury with intact skin. These are the circumstances usually encountered. If skin and soft tissues are torn and the cartilages fractured or dislocated, these tissues may be replaced and sutured through the external wound before its closure. The indwelling plastic tube must always be used to maintain any open reduction or suture.

Late Treatment

Sometimes the patient with laryngeal trauma is not seen by the laryngologist for

two or three weeks following the injury. In such an instance the first step in treatment is a direct laryngoscopy and passing of the largest possible bronchoscope in an attempt to "iron out" any dislocation. This has been successful in a few cases as late as three weeks after the injury. If it is not successful or the patient comes to the otolaryngologist much later, an indwelling section should be placed. Usually there is a tracheotomy and its opening is enlarged upwards as high as the lower border of the cricoid cartilage in order to allow inspection, the carving out of scar tissue and the placing of the largest possible section. Skin grafting of such a dissected out area is not indicated unless there is very large or completely circumferential baring of submucosal tissues.

A tear of just the hypopharynx or pyriform sinuses or cricopharyngeal area has been indicated when air was noted by crepitus or X-ray examination to be only in the posterior pharyngeal or prevertebral areas. These patients have no embarrassment of their airway and need only the placing of a nasopharyngeal feeding tube. Lower tears of the upper esophagus have been missed because all attention had been focused upon the fractured and dislocated larynx which had necessitated a tracheotomy. In some of these patients attention was directed to the esophagus because of great pain, dysphagia

and evidence that food was entering the tracheobronchial tree.

In a few patients paralysis of abduction has persisted even after the laryngeal and subglottic tracheal airway was reestablished. This has necessitated arytenoidectomies or arytenoidopexies.

Summary

It is stressed that the otolaryngologist, if possible, will do a direct examination and institute treatment when he first sees the patient. An attempt should be made with the largest possible bronchoscope to "iron out" any dislocation of the larynx. The use of indwelling laryngeal sections will maintain the realignment of fractured parts. The demonstration of large tracheal tears or cartilaginous separation necessitates open surgery with repair and placement of sections. Painful and difficult swallowing with pooling of saliva, blood, and drooling usually denotes a tear of the hypopharynx or pyriform sinuses. The use of an indwelling nasal feeding tube may be needed for these patients. Most tears of the esophagus necessitate open surgery and repair. The use of continuous dilation and realignment of fractured and dislocated cartilage by the use of the indwelling sections has obviated the use of other procedures, such as open reduction and sleeve resections.

Types of Obesity

Pleasingly Plump

A nice, convenient classification of obesity might be first, just mildly obese, which should refer to the pleasingly plump individual who does not stick out too much here and there, and who may realize that it is better to prepare and prevent than to repair and repent.

The Stout Type

The second degree of obesity could be termed the stout or corpulent type who bulges fore and aft. He usually wheezes and puffs, and is forever trying to impress his audience with his light-footedness in spite of his flat-footedness.

As Viewed from the Mirror

And last, there is the really fat individual, whose chins are a part of his chest, and if he does happen to move, he flows. He has given up trying to be thinner even next year, and has also given up the inspection of his hidden bodily acres that he can view only with a mirror.*

*F. William Saul, M.D.: Pink Pills for Pale People.

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Precautions: Use with caution in patients hypersensitive to sympathomimetic compounds, who have coronary or cardiovascular disease, or are severely hypertensive.

Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side Effects: Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness.

Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.



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Venereal Disease A Serious National Problem, Says AMA

Venereal disease is spreading so rapidly that it now represents this nation's most urgent communicable disease problem.

VD is hitting particularly hard among teenagers and young adults, according to the American Medical Association.

The venereal diseases are infecting about two Americans a minute—3,000 a day, or 1,100,000 a year. Cases of infectious syphilis have almost tripled in this country in the past five years. More than a million

new cases of gonorrhea are developing annually.

VD can blind, cripple, and even kill.

The ravages of venereal diseases are all needless tragedy, says the AMA, because both syphilis and gonorrhea can be avoided. If contracted, they can be cured by prompt medical treatment.

The cure for both diseases—penicillin—has been available since 1943. Any family physician or public health clinic can administer

prompt treatment.

Venereal disease is caused by intimate personal contact.

Complacency, ignorance, and a free-and-easy attitude toward moral standards are partly responsible for the spread of VD; the increasing use of alcohol, especially among young people, also plays a role.

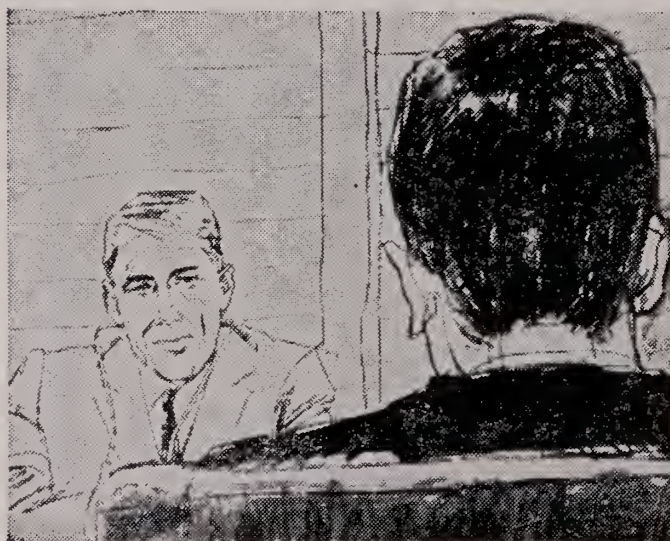
Authorities believe, however, that thousands of young people simply aren't aware of the dangers of VD. Once infected, they are complacent about treatment.

One of the first signs of syphilis may be a painless, ulcerating sore. Gonorrhea produces inflammation of the genital and urinary tracts, and a discharge of pus.

A person may contract syphilis and be unaware that he has the disease. After the first symptoms, the germs may remain hidden in the body for as long as 20 years before any damage is discovered. Then the person may become crippled, develop heart disease, blood vessel disease, blindness, or show mental symptoms. Even death may result from this hidden stage of syphilis.

If left untreated, gonorrhea may be responsible for arthritis, endocarditis, sterility, and blindness.

If a person suspects he may have contracted venereal disease, he should go to a physician immediately.



VD should be treated promptly by a physician.

Endolaryngeal Removal of Benign Tumors

FRANCIS E. LEJEUNE, SR., M.D.*
New Orleans, Louisiana

ENDOLARYNGEAL REMOVAL OF benign tumors of the larynx may be accomplished by indirect or direct laryngoscopy. Considerable skill is required to remove small tumors, such as polyps, papillomas, or granulomas, from the vocal cords by the indirect method. Not only is thorough cocainization of the hypopharynx and larynx necessary, but for successful removal the patient must be cooperative and tolerant. For this reason, relatively few tumors of the vocal cords are removed by indirect laryngoscopy.

Direct Laryngoscopy

Direct laryngoscopy offers possibilities of greater success in the removal of tumors of the larynx. Endolaryngeal surgical procedures entail use of a laryngoscope, which permits a direct and satisfactory approach to the larynx. Several types of laryngoscopes are available for direct exposure of the larynx. Undoubtedly, the most popular type in this country is the Jackson laryngoscope or one of its modifications. It provides a beautiful view of the larynx and usually requires only local anesthesia. With this laryngoscope the larynx is approached through an opening about the size of a dime. Surgical removal of a tumor from the vocal cords requires use of a forceps and only one hand. With one-handed surgical removal of these tumors, however, it is always possible to tear or strip the vocal cord mucosa.

Suspension Laryngoscopy

Another method, which is used by relatively few laryngologists, is suspension laryngoscopy. It offers an unexcelled approach to the larynx through a wide open mouth and permits use of both hands to remove the growth. It is our method of choice for endolaryngeal surgical procedures.

Suspension laryngoscopy is best done with

*Department of Otorhinolaryngology, Ochsner Clinic, New Orleans.

the patient anesthetized with sodium pentothal and curare as described by Welborn.¹ After the patient is completely anesthetized, the suspension laryngoscope is introduced into the mouth, and the larynx is exposed to direct vision. By sitting at the head of the table and projecting a beam of light into the mouth, the surgeon can view the hypopharynx and larynx satisfactorily in most patients. With a laryngeal spatula the vocal cords can be retracted for better visualization of the tumor, and palpation can be carried out as desired.

Retraction of the ventricular band provides better visualization of the ventricular area. If a polyp or small papilloma is to be removed from the edge of the cord, the tumor is grasped with a Yankhauer-Little forceps and, while slight traction is made to the opposite side, the tumor is excised by sharp dissection with a laryngeal knife in either the right or the left hand, depending on the location of the tumor. We have found that a #11 Bard-Parker blade sharpened on both edges gives excellent results.

With suspension laryngoscopy the approach to the larynx is limited only by the size of the mouth. We have found through the years that the larynx is much easier to expose and visualize in edentulous patients.

Laryngeal Polyps

In our experience the most frequent growths in the larynx and on the vocal cords are polyps. These are not true tumors but are inflammatory reactions and in their early stages may disappear spontaneously. At times, however, they attain considerable size. When persistent, they must be removed surgically. If removed accurately and with as little trauma to the vocal cord as possible, little or no impairment of vocal function will result. This is also true of other types of benign growths.

Papillomas of Childhood

The most frequent tumors of the larynx found in little children are vocal nodules and multiple papillomas. Unless severe hoarseness is present, vocal nodules in children are not removed until the child has reached the age when cooperation is assured.

Multiple papillomas of the larynx are the most feared tumors in children. These growths seem to have a predilection for the underprivileged child.

Because of the excellent exposure, wide approach to the larynx, and use of both hands, suspension laryngoscopy offers the best means for removal of this type of growth. Pinching or scalping off the papillomas with the Yankhauer-Little forceps, caution being exercised not to bite into the substance of the cord or mucosa of the larynx, has given us the best results. If this technic is followed, it is rewarding to see, when papillomas no longer recur, vocal cords that appear quite normal in spite of multiple operations for removal of these growths.

Papillomas after Puberty

It is generally believed that multiple papillomas disappear about the age of puberty; but this is not always true, since we have seen adults who stated that they had had these growths since childhood. Multiple papillomas may develop in adult life and recur in a manner similar to the way they do in children. An interesting observation was disappearance of papillomas from the vocal cords and larynx in three patients during pregnancy. Shortly after termination of the pregnancy the papillomas recurred. From a research point of view this observation is significant.

Contact Ulcer Granulomas

Aside from specific granulomas, two types of granulomas are occasionally seen in the larynx. Contact ulcers, which always occur at the vocal process, may be unilateral or bilateral and are due to overuse of the voice. The mucosa covering the vocal process is extremely thin, and when traumatized by the opposite process, becomes ulcerated; infection follows and granulating tissue soon appears. With the aid of suspension laryngoscopy the posterior portion of the larynx is easily exposed to direct vision, and the granulating tissue is removed with forceps, care being exercised not to injure the arytenoid cartilage. Vocal rest is imperative.

Although the granulations recur with considerable frequency requiring removal, I have never seen a case that eventually did not clear up.

Intubation Anesthesia

Progress in medicine is responsible for another type of granuloma which began to be encountered shortly after introduction of intubation anesthesia. Granulomas occasionally develop after long intubation anesthesia. They may be unilateral or bilateral. The most common site is the vocal process, but occasionally they develop in the middle third of the vocal cord. Unlike granulomas occurring in conjunction with contact ulcers, intubation granulomas as a rule do not recur after removal.

Polypoid Degeneration

Bilateral polypoid degeneration of the vocal cords is characterized by extensive polypoid tissue on the contact surface of the cords extending from the anterior commissure and ending abruptly at the vocal process. It develops from constant irritation, possibly owing to excessive talking and smoking. The polypoid tissue is soft and baggy and at times so extensive as to cause over-

riding of each cord with resultant increased hoarseness and mild dyspnea. Because of faint transparency of the tissue it is often possible to see the edge of the true vocal cord through the polypoid tissue. Though extremely friable, this tissue can be grasped with forceps and, with slight traction to the opposite side, excised along the edge of the cord with a sharp laryngeal knife just short of the anterior commissure. The opposite cord is treated in the same manner, care being exercised to leave a small amount of polypoid tissue at the anterior commissure. This, of course, is done to prevent formation of a web at the anterior commissure.

Benign Tumors

Other benign tumors of the larynx, such as fibromas, hematomas, cysts, and angiomas, are removed by the same technic as previously described. If bleeding persists after removal of any of these tumors, the bleeding vessel is electrocoagulated with the Cameron pistol grip combination of suction and cautery. Cysts of the epiglottis, occasionally extremely large, are dissected free and, after removal, the mucosa is approximated and sutured effectively to cover the raw areas. This type of suturing is possible only with use of suspension laryngoscopy.

Reference

1. Welborn, S. G.: Anesthesia for Suspension Laryngoscopy; Experience with 552 Cases. *Southern Med J* 58:244, 1965.

Surgery in the Bible

This is my covenant, which ye shall keep, between me and you and thy seed after thee; Every man child among you shall be circumcised.

And ye shall circumcise the flesh of your foreskin; and it shall be a token of the covenant betwixt me and you.

And Abraham took Ishmael his son, and all that were born in his house, and all that were bought with his money, every male among the men of Abraham's house; and circumcised the flesh of their foreskin in the self-same day, as God had said unto him.

And Abraham was ninety years old and nine, when he was circumcised in the flesh of his foreskin.

Genesis 17:10, 10, 11; 22, 23.

Derivatively Speaking

ARTERY is derived from the two Greek words *aer* (air) and *terrein* (to keep), because the Greeks thought that the arteries like the windpipe contained only air. Though Galen later found that the arteries were not empty but conveyed blood, the name artery persisted.



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The Role of the Respiratory Mucosa

In
Health
and
Disease

A. C. HILDING, M.D., Ph.D.*
Duluth, Minnesota

THE RESPIRATORY MUCOSA, together with its mucous blanket is in effect a vital organ which, fortunately, has recently been receiving some measure of the attention which its importance warrants. This has not always been the case.

Respiratory Mucosa

The respiratory mucosa can be said to line the entire tract from the vestibule of the nose to the alveoli, including the eustachian tube, the middle ear, the mastoid, and the sinuses. It is usually thought of as being ciliated and so it *is*, in the posterior two thirds of the nose, eustachian tube, sinuses, and tracheobronchial tree, at least as far as the terminal bronchioles, and sometimes into the respiratory bronchioles. It is by no means a uniform structure, however, but varies greatly according to its exposure to air flow. In the anterior portion of the nose, where it is exposed to unconditioned air entering the anterior nares, it is of the thick, squamous type. The air enters with a high velocity in the form of jets directed more up than back. Other areas that are normally covered by squamous epithelium include the pharynx, portions of the epiglottis, the ary-epiglottic folds, and the vocal cords. In addition, in otherwise normal people, squamous islands frequently occur in the tracheobronchial tree. Non-ciliated also is the mucosa of the middle ear, the mastoid, and the portion of the lungs distal to the respiratory bronchioles. In these areas the epithelium flattens out until it approaches endothelium in appearance. In fact, it becomes so thin in the alveoli that for a time its very existence was questioned. Recalling that the alveoli are said to contain an area as large as one or two tennis courts, and including the lining of these areas as respiratory mu-

*From the Research Laboratory, St. Luke's Hospital, Duluth, Minnesota. Work supported by United States Public Health Service Research Grant No. GM 09603-03; work sponsored and housed by St. Luke's Hospital, Duluth, Minnesota.

cosa, it follows that by far the greatest portion of the respiratory mucosa is non-ciliated.

Mucous Blanket

Throughout the whole tract, upper and lower, the mucosa is overlaid by an intact blanket or lining of mucus that is completely changed many times a day. This system is something like an escalator or belt conveyor, the cilia supplying the motive power, and the mucous blanket being the conveyor. This mucous blanket is referred to as the ciliary stream.

The Nose

In the nose the ciliary stream moves very slowly over the squamous areas in the anterior third (1 or 2 mm./hr.); in the rest of the nose it moves relatively fast (about 10 mm./min.), and it leaves the nose posteriorly on the lateral wall of the pharynx. The whole drainage from the lateral wall of the nose forms a rather narrow stream which divides around the eustachian orifice. It is here that the ciliated epithelium ceases, the mucosa becomes squamous in form, and the swallowing mechanism takes over the drainage. In the lower tract the mucous blanket is thinner (less deep) in the small bronchi than in the trachea, and becomes shallow to the vanishing point in the alveoli. But even here there is some mucin in the secretion, and it is thought that drainage is accomplished slowly by means of traction, with respiratory movements perhaps playing a part.

The Alveoli

Another physiologic mechanism in the alveoli, the surfactant, keeps the alveoli open and the lung uniformly expanded, even though the alveoli, saccules, and atria are of different sizes and shapes. This surface-active material is thought to be a phospholipid and has the property of changing surface tension in such a way that, as the alveoli are distended in inspiration, the surface tension increases, whereas, as the alveoli grow smaller in expiration, the surface tension decreases, until it practically reaches

zero. If the alveoli were lined by a water layer, the reverse would be true: the surface tension would decrease as the alveoli expanded, and increase so greatly as they contracted, that they would be likely to collapse, causing atelectasis.

Tracheobronchial Tree

The ciliary stream in the tracheobronchial tree might be likened to an upside-down river. In this picture, the alveolar areas (one or two tennis courts of them) represent the meadows in the drainage system; the water there is not easily visible and moves slowly toward the river. The respiratory and terminal bronchioles would correspond to the rivulets in which small streams of water can be seen flowing slowly, later joining to make brooks, and, eventually, the river. So the bronchioles unite into larger bronchi, and eventually the trachea (our river). Both in the geographic river and in the ciliary stream, the stream-bed grows progressively narrower and the depth and volume of the flow progressively greater. In the short distance from the periphery of the lungs to the bifurcation, the stream-bed of the ciliary flow narrows from meters to 5 cm. — the circumference of the trachea.

Obstructions

Just as the geographic river encounters obstructions in the form of sand bars and islands in its course, so the ciliary stream meets obstructions. The opening of each tributary bronchus becomes an obstructing island around which the mucus must flow. Thus, at the upstream margin of each bronchial opening, the mucous blanket must cease its axial flow, split, and change direction to go around the opening. Recalling that there is a similar blanket coming from the tributary bronchus, which also must split on the carina where the two bronchi join, one would readily understand that here is a four-way split in the blanket, with probably some slowing of flow. When squamous islands occur, they are apt to be found on the crests of carinas. These and squamous islands located elsewhere may not stop the flow, because the blanket is dragged across

by adjacent cilia, but there is likely some slowing at such points. Again, at the squamous-covered vocal cords, the ciliary stream meets obstruction, and the blanket coming up the anterior wall of the trachea must cease its axial progress, as at a jettie. The mucous blanket must split at the anterior commissure, as the direction of flow changes from axial to transversely backward, as it follows the cord margin.

Changes with Development of Disease

This then is a brief description, as it is found in health, of the barrier-mechanism that stands between us and that part of our environment that we breathe. When disease develops as a result of its exposure, secretions may be increased a hundred-fold, the thickness of the mucosa enormously increased, and its character entirely changed.

Eighteen times a minute we breathe air that varies widely as to temperature, humidity, and air ion content. This barrier-mechanism must not only prepare the air for reception in the lungs but also conduct it there. The air may contain a wide variety of community and industrial pollutants, odors — pleasant and otherwise, dust — both organic and inorganic, bacteria, viruses, and pollens. The nose warms and humidifies the incoming air very effectually, but dust filtration there is not complete.

Deposition

Deposition of particulate matter results from the interplay of a number of forces: inertia, velocity, air friction, gravity, and diffusion. Practically all particles 10 microns or more in diameter, most 5 microns, and a substantial percentage of those measuring 2 to 5 microns in diameter are deposited in the nose. This deposition is due largely to velocity, inertia, and gravity. Below 2 microns, these forces are not effective. Neither is diffusion, which does not take over until the particle size is less than half a micron. Thus between 0.5 micron and 2 microns, deposition is at its lowest point (20 to 30 per cent) and filtration least effective. Below

0.5 micron, deposition increases again, and all particles less than 0.1 micron in diameter are deposited by diffusion. In addition to size, the shape of particles and specific gravity have a bearing.*

Particles deposited in the alveoli are removed through "sump pores" and taken into the lymphatic system (with or without phagocytic action), or they may be picked up by "dust cells", macrophages, in the alveoli. These cells find their way upward to the terminal bronchioles, where they either disintegrate, dropping their load of particulate matter, or are carried out intact in the mucous blanket.

Fate of Deposited Particles

The fate of the particle itself, the damage it does to the cell, and the reactions of the cellular tissue depend upon the nature of the particle. Some may be dissolved and absorbed quickly (almost as quickly as some gases) and have an immediate general effect. Some inert ones may be removed completely and harmlessly, and others which dissolve slowly may affect the underlying cells more or less severely as they move along, depending upon the intimacy and duration of the contact.

Carcinogenesis

Contact time is increased where the ciliary stream is slowed. This is thought to be the key to the location and genesis of malignancy in the tract. Nasopharyngeal carcinoma arises high on the lateral wall of the pharynx, where the ciliary stream coming from the nose meets squamous epithelium in Rosenmüller's fossa. This is thought to explain the high incidence of this type of carcinoma in Chinese people. They are said to have certain fibrous bands, which span Rosenmüller's fossa and are not found in Europeans. In the lower tract, squamous islands in the bronchi, especially on the crests of carinas, and the vocal cords are points of slowing. Squamous cell carcinoma of the larynx is prone to occur in the anterior portions of the vocal cords, and the most active part of such carcinomas is the anterior portion.

*For those who are interested in this subject, a comprehensive text, *Pulmonary Deposition and Retention of Inhaled Aerosols* has been written by Hatch and Gross (Academic Press, New York).

Bacteria and Viruses

If the deposited particulate matter consists of bacteria and viruses, the effect upon the underlying cells and the tissue reaction will depend upon the nature of the organism. The viruses of the common cold, of which there are 30 to 40, and of influenza are common ones which attack the respiratory mucosa. Typically, they invade the mature columnar cells, forming inclusion bodies in or near the nucleus, after which these cells exfoliate. Such exfoliation may reduce the epithelium to a single layer of replacement cells next to the basement membrane. From these cells the epithelium must be rebuilt and, during this process, the epithelium is probably quite susceptible to infection by bacteria.

Minimal Surface Trauma and Epithelial Repair

The exfoliation of the epithelium was imitated, to a degree, in experiments in which the surface cells were subjected to minimal mechanical damage. In these experiments, it took from five to seven days for the epithelium to rebuild. The last to be replaced were the cilia. These develop from centrioles, the same centrioles which take part in mitoses, but, instead of replicating themselves once, as in mitosis, to form two cells, they replicate themselves scores of times, to form scores of cilia on a single cell.

Pollens

Pollens may penetrate the epithelium with their well known effect. In this condition, however, there is little or no exfoliation.*

Industrial Fumes

The effect of industrial fumes depends upon their natures and their solubilities.

Under certain conditions, the mucociliary system may be so completely destroyed that a fatal outcome is likely. This occurs in chronic disease such as severe asthma, in acute infections like laryngotracheobronchitis, and in chemical destruction, as from war gases or other inhaled chemicals. Under

such circumstances, the patient may die from mucociliary insufficiency unless special measures are taken to get air into the lungs and to get secretions removed, until the epithelium can begin to repair.

Genetic Disease

Not all diseases of the respiratory mucosa are due to inhaled noxious materials or local infections. Some are due to general metabolic disease; others are genetically determined, such as hyaline membrane disease and cystic fibrosis.

Cigarette Smoke

Cigarette smoke is a unique form of air pollution which, among those who smoke cigarettes, far exceeds all commercial and community pollution combined. This form is characterized as "personal pollution." It is purposefully and willfully produced. Unlike other forms of pollution, it does not pass through the nose to be partially filtered. (In experimental animals, it has been found that the nose filters out at least a third of the chloroform-soluble constituents of cigarette smoke.) It is taken directly into the mouth in a form so unbelievably dense that one cannot appreciate it unless he actually watches the business end of a cigarette, as it delivers its charge, under the conditions of time and pressures used by smokers in taking their "drags." Typically, a cigarette smoker takes about 35 cc. of the dense smoke into his mouth and then, in the pharynx, feeds it into the next incoming flow of inspired air, some 500 cc. Most smokers exhale again, before it is all deposited. Roughly half is retained. There are, however, wide variations in the habits of smokers, that is, the manner in which smokers handle the charge after receiving it in the mouth. Some small number puff it out again, as do typical pipe smokers, in which case it does not enter the respiratory tract at all and its damaging effects are slight. Others open the mouth and take a big breath through the mouth, thus driving the whole undiluted charge right down to the alveoli, then hold the breath for a few seconds, until it all deposits. Five seconds is usually

*Acute and chronic infection and allergy are discussed elsewhere in this issue.

enough to accomplish complete deposition of visible smoke. There are all variations of habit between these two extremes.

The resulting effect upon the respiratory tract depends not only upon the temperature of the burning coal at the end of the cigarette, but upon "how much and how often."

The different chemical compounds that have been found in cigarette smoke are so numerous that it takes pages to list them. The mucociliary mechanism does exceedingly well in clearing out a large part of these smoke materials. However, there are many compounds with which it cannot cope and some which it handles indifferently well. Some of the components of the gaseous phase are very quickly absorbed and quickly exert an effect upon the whole body, for instance, nicotine and carbon monoxide. Much of the tar is apparently removed by ciliary action, but some of the components, nevertheless, injure the epithelium and cause chronic trouble. Among smokers, squamous areas are very much more common than among non-smokers, and these seem to occur commonly at the four-way split in the mucous blanket, on the carinas. At this point also, radioactive polonium, contained in cigarette smoke, accumulates in quantities far above what it does on the smooth walls of the bronchi. Lung cancer commonly occurs in the medium-sized bronchi, supposedly beginning in squamous islands. More than three quarters of the lung cancers are found among cigarette smokers. Cancer of the vocal cords, as described earlier, is likewise prone to occur in cigarette smokers.

Among other effects, cigarette smoke is ciliostatic. There are a number of compounds in both the tar and the gaseous phases which have the effect of slowing or stopping ciliary action. This hampers lung clearance. Eventually some areas, presumably those which get the brunt of smoke effects, take refuge in a squamous form of epithelium. This does not necessarily mean that all such areas will develop malignant change, but it seems fairly clear that a developing malignancy goes through this stage. The steps of the change from well-ciliated, columnar epithelium to squamous epithelium have not been spelled out. Be that as it may, chronic conditions develop, characterized by increased production of viscid secretion, invasion by bacteria, bronchitis, and emphysema, with all the museum of pathologic conditions found in those two related diseases. In this country we are experiencing a very rapid rise in the incidence of chronic bronchitis and emphysema, very largely among smokers. The most effective therapy seems to be cessation of smoking.

Conclusion

To discuss adequately the subject of this paper, one would produce enough volumes to fill a library, but perhaps these few comments may serve to emphasize the importance of the respiratory mucosa. Fortunately, its role is currently being studied more than ever before. Even the lay press knowledgeably discusses emphysema, ciliostasis, and hyaline membrane disease. As to advertisers — one might think that some live on self-diagnosed sinusitis!

A Pioneer Greek Surgeon

Antyllus (2nd Century) was the creator of arterial surgery, and was the first to distinguish aneurysm caused by pathological dilatation and aneurysm forming after trauma of the artery. When he treated a circumscribed distention of the arterial wall by ligating the aneurysm above and below the pulsating sac, followed by opening the aneurysm and evacuating its bloody contents, he projected his name to the present time, for the method of Antyllus is still pictured in the textbooks and defined in the dictionaries.*

*Victor Robinson: *The Story of Medicine*.

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Pharyngeal and Esophageal Dysfunction

The Diagnosis

JOHN A. KIRCHNER, M.D.*
New Haven, Connecticut

THE PHARYNX and esophagus form a channel for transporting ingesta from the mouth to the stomach. Since the pharynx also admits inspired air on its way to the larynx and lung, breathing is reflexly arrested for a moment during swallowing. The airway is further protected by the laryngeal sphincter mechanism and by the valleculae and pyriform sinuses which act as temporary reservoirs for residual ingesta after the first swallow is completed. Fluids are rapidly moved from the mouth to the esophagus by the "squirt mechanism" produced by the upward pressure of the tongue against the soft palate and faucial arches. The pharyngeal walls have little or no effect on the passage of thin liquids into the esophagus. Solids are conveyed through the pharynx by a contraction wave which passes from the mouth down through the muscular walls of the pharynx and merges with the esophageal peristaltic wave which follows.

Pathophysiology

Disorders of deglutition can result from muscular dysfunction anywhere along the oral-pharyngeal-esophageal tract. The mechanism of the disorder usually becomes evident as the patient reports his symptoms, although he may not complain primarily of dysphagia. For example, excessive mucus and cough may be due to laryngeal flooding from a paralyzed, dilated pyriform sinus, or from a pharyngeal diverticulum. Usually, however, the patient can localize the level of the disorder if the physician helps with a few questions directed at the oral, pharyngeal and esophageal stages of swallowing.

Patient Evaluation

History

Is there any difficulty in moving food or liquid from the front of the mouth to the

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throat? The oral stage of deglutition depends on normal function of the tongue, soft palate and suprahyoid muscles.

Do liquids escape from the nose during swallowing? This would indicate a weakness of the soft palate or superior constrictor muscle. Do fluids cause coughing or choking? Paresis of one or both sides of the hypopharynx can produce these symptoms. They are often accompanied by hoarseness or vocal weakness as a result of ipsilateral vocal cord paralysis.

Is there a gurgling sound in the throat? This suggests diverticulum of the hypopharynx, as would a report of regurgitating food eaten some time previously. A diverticulum may also cause coughing spells during the night, when the patient is recumbent and the pharyngeal muscles relaxed.

Is it necessary to perform several attempts at swallowing before food descends into the esophagus? This is sometimes an early manifestation of myasthenia gravis.

Do solid foods get caught somewhere between the throat and the stomach? The patient can usually point to the level of obstruction. This may be due to stricture, neoplasm, pressure from adjacent masses (substernal thyroid, aortic aneurysm or cardiac enlargement) or neuromuscular disorders such as achalasia.

One should ask whether pain is present, whether it is related to intake of food or fluids, and whether it is referred to the ear or neck.

Recent weight loss is common with organic disorders of deglutition, but absent in globus hystericus, a common complaint among tense young women. The choking sensation in this condition does not produce coughing or aspiration, nor does it interfere with swallowing food. Careful inquiry into the patient's way of life usually reveals several possible sources of emotional tension.

Clinical Examination

Physical examination of the patient with dysphagia should begin with an assessment of the patient's voice and speech as he relates his symptoms. Dysarthria or hypernasality should indicate the need for careful

examination of the structures supplied by the cranial nerves, especially nine through twelve. The patient with a recent vocal weakness or hoarseness should be asked to cough. Vocal cord paralysis often makes coughing impossible.

Palpation of the neck may reveal an enlarged, low-lying thyroid gland as a cause of the choking sensation or dysphagia. Deviation of the larynx or trachea from the midline may occur in either paralysis of the constrictor muscles or an enlarging soft tissue mass in the hypopharynx. Digital pressure against the posterolateral aspects of the cricoid ring may disclose moderate tenderness of the cricopharyngeus muscle in globus hystericus.

Inspection of the neck during performance of Valsalva maneuver may identify a bulging pharyngocele or laryngocele, or a dropping forward of the larynx in case of weakness of the supporting constrictor muscles.

Auscultation is occasionally helpful in identifying a pulsion diverticulum.

The intra-oral examination may reveal weakness of the tongue, soft palate or pharyngeal walls. Deviation of the uvula during phonation usually indicates a neurological deficit of the vagus nerve, as does an asymmetrical movement of the posterior pharyngeal wall.

Inspection of the pharynx by mirror is usually the most revealing part of the physical examination. It may show saliva lying puddled in one pyriform sinus, indicating paresis of the inferior constrictor muscle, usually due to a high lesion of the vagus nerve trunk or nucleus ambiguus. In such cases the vocal cord of the same side is usually paralyzed and lies in a partly abducted position. Saliva can sometimes be seen spilling over from the pyriform sinus into the larynx.

Saliva lying in both valleculae and in both pyriform sinuses is often seen in pseudobulbar palsy or in other disorders of the bulbar nuclei.

Indirect Laryngoscopy

Mirror examination should include at least a quick look at the vocal cords. Rotation of

the glottic chink is often seen in unilateral vagal paralysis, the posterior commissure being displaced toward the side of the paralysis. A difference in position of the two arytenoid cartilages sometimes identifies a unilateral paralysis of the vagus or the recurrent laryngeal nerve, as does a failure of one vocal cord to move briskly or at all. Remarkably enough, these deviations from the normal laryngeal appearance may also be produced by carcinoma of the pyriform sinus or the post-cricoid area. Tumors in these two areas are often beyond the view of the laryngeal mirror and must be found on radiological or endoscopic examination.

X-Ray Examination

A careful radiological examination is prob-

ably the most important single measure in the evaluation of pharyngeal or esophageal disorders. The passage of a barium suspension through the pharynx and esophagus can be observed on an image intensifier and recorded on motion picture film or video tape.

A thin barium suspension passes rapidly through the normal pharynx and esophagus, leaving no residue. A thick suspension is moved along more slowly by the oral and pharyngeal musculature until it is taken by the esophageal peristaltic wave and carried to the stomach. The action is filmed in the anteroposterior and lateral views, with the patient upright. If paresis is suspected, the examination is repeated with the patient in the supine position. The thick barium mixture coats the walls of the mouth and

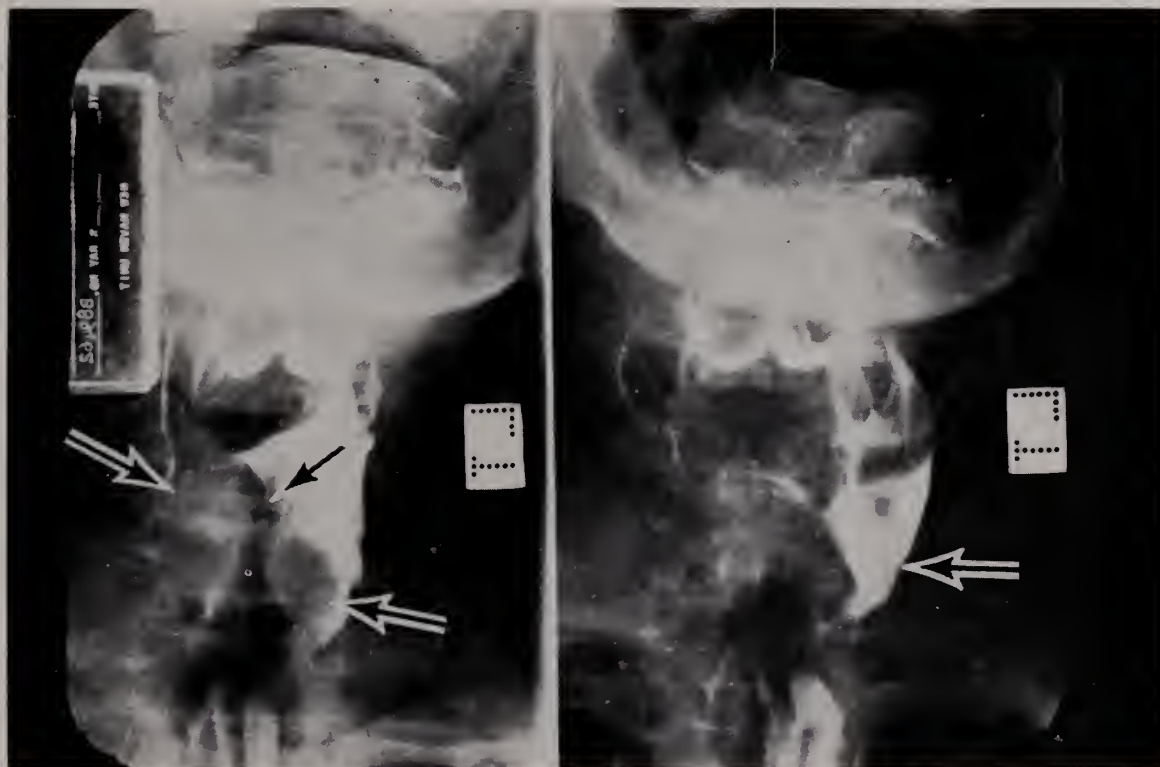


Figure — Sixty-eight-year-old man with three-week history of hoarseness and dysphagia. Left vocal cord paralyzed. Saliva pooled in left pyriform sinus. Frequent spells of coughing.

Film on left demonstrates the pattern which was initially interpreted as a soft-tissue mass in right hypopharynx (outlined by arrows). Valsalva maneuver on right film shows dilatation of the left pyriform sinus (arrow), indicating paresis of the left inferior constrictor muscle and inability of the left pyriform sinus to empty itself.

Cinefluorography showed that both pyriform sinuses filled completely and evenly during the passage of the barium suspension. This would not occur in the presence of a tumor in this area.

Residual saliva, pooled in the left pyriform sinus, spilled over from time to time into the larynx and produced spells of coughing.

During the following few months, progressive atrophy of the muscles of the neck, shoulders, mandible and limbs occurred. A diagnosis of amyotrophic lateral sclerosis was made before the patient died.

pharynx, allowing easier identification of masses, diverticula, ulcers and areas of asymmetry.

Study of the pharynx should include a swallow with the head turned to the right, and to the left. Turning the head to one side directs the barium into the opposite pyriform sinus, demonstrating its patency and freedom from tumor. Since some people use one pyriform sinus exclusively when swallowing small amounts, a large mouthful of the barium mixture should be given.

Valsalva Maneuver

Another useful technique in examining the pharynx is to have the patient perform the Valsalva maneuver after the pharynx has been coated with barium. This consists of a forced expiratory effort against a closed mouth and nose, and may show the outlines of a mass in the pharynx, or it may demonstrate ballooning of the atonic side in unilateral pharyngoplegia (Figure).

The esophagus is similarly examined with the barium suspension for retained fluid contents; dilatation (as with achalasia* or stric-

ture); rigidity and lack of peristaltic contractions (scleroderma); tertiary contractions (purposeless and nonpropulsive, seen in the aged); areas of extrinsic pressure, intrinsic masses, fibrous ring or hiatus hernia at the cardiac end, and other abnormalities.

Direct Laryngoscopy

Endoscopic examination of the pharynx and esophagus allows more precise visualization or biopsy of areas which are inaccessible by mirror examination. These areas include the pyriform sinuses, the retro-cricoid area of the hypopharynx, and the esophagus itself.

A diagnostic technique which has gained favor in recent years is the measurement of pressures developed within the pharynx and esophagus during the act of swallowing. The patient simply swallows the end of a small triple-lumen polyethylene tube which is filled with water and attached at its upper end to three pressure transducers and a direct writing recorder. Pressure patterns characteristic of normal peristalsis, diffuse spasm, achalasia, scleroderma and similar disorders can be recognized.

*See Test Your Word Score Page 1028.

Sickle Cell Anemia — Genesis

At one conference a case of sickle cell anemia in a child of Italian parentage was shown. A discussion of sickle cell anemia in people who live in the countries bordering the Mediterranean sea followed. Dr. Schick pointed out that, after all, Africa is not very far distant from Italy. The pediatric resident said, "Yes, the family had lived in Sicily but there had been no contact with the Negroes, except possibly one day a year, when the circus came to town." Dr. Schick replied tersely. "One day is enough."*

*I. J. Wolf, M. D.: *Aphorisms and Facetiae of Bela Schick*.

Ten Commandments For Patients

1. Select your doctor carefully.
2. Don't desert him if you find him satisfactory.
3. Ask him questions.
4. Follow his prescriptions.
5. Don't cheat him.
6. Don't expect witchcraft.
7. See him while you are healthy.
8. Assist him as a partner.
9. Keep your own health file.
10. Respect his time and work.

— Martin Gumpert, M.D., *You and Your Doctor*, Bobbs-Merrill, 1952.

|| Tracheotomy

ROBERT E. PRIEST, M.D.*
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TRACHEOTOMY WAS first described just after the beginning of the Christian era; however, the increased prevalence of diphtheria in France in the first quarter of the 19th Century was responsible for the final and convincing demonstration of the possibilities of tracheotomy by Bretonneau and Trouseau. Before the 19th Century, tracheotomy was contemplated only when suffocation was imminent.

In 1546 Brassavola, an Italian physician, described opening the trachea of a boy who was nearly dead from an "abscess in the windpipe." This seems to be the first recorded successful case.

Part of the account of the first tracheotomy performed in Great Britain by George Martine of St. Andrews in 1730 states: "Upon the Subject I should not have had so much to say if this elegant Method of rescuing one from imminent Danger, and the most difficult kind of Death, had not been ordinarily described more from Theory than from Practice, and if Surgeons had been half as bold as to assist Nature in such an Extremity as they are officious to disturb her regular and salutary steps."

The technique of tracheotomy evolved slowly. The first surgeons who performed this operation were afraid to incise cartilage because it was known to heal slowly. They used a transverse incision in skin and trachea.

Tracheotomy tubes were straight and short at first (Fabricius, 1619) and were so illustrated as late as 1795 (Latta's "Surgery"). Casserius (1561-1616) suggested a curved tube with holes in all directions. Sanctorius (1561-1636) advised a straight trochar such as is used in tapping a hydrocele. Martine (1730) was certainly the first to mention a double walled tube, but he does not say that he used it.

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Use in Bulbar Polio

Until 1930 tracheotomy was reserved for cases of respiratory obstruction at or above the level of the larynx, but Wilson, in 1932, and Davidson, in 1936, suggested tracheotomy for the relief of respiratory insufficiency due to the bulbar form of poliomyelitis, according to Cawthorne. About this time tracheotomy was suggested as an alternative to repeated bronchoscopy for the removal of secretions in acute laryngotracheobronchitis in children. Galloway, in 1943 and 1947, advocated tracheotomy in various childhood respiratory diseases including bulbar poliomyelitis.

In 1947 Priest, Boies, and Goltz summarized their experiences with tracheotomy in patients with bulbar poliomyelitis treated at the University of Minnesota Hospitals and the Minneapolis General Hospital during the 1946 epidemic.

As a result of this experience, they said: "We believe that tracheotomy has an important place in the treatment of bulbar poliomyelitis. In certain patients, we think it is a life-saving procedure. There is reluctance on the part of some physicians to accept tracheotomy as a useful adjunct in the treatment of poliomyelitis. Any physician whose experience with bulbar poliomyelitis encompasses only a few cases may question the need for tracheotomy. However, an epidemic in which several hundred bulbar cases occur produces a considerable number which meet the criteria for tracheotomy as outlined in this paper."

Five years after the 1947 publication, Priest, Boies, Goltz, Younger, and Koller undertook to review the world's literature to assess the opinions expressed therein concerning tracheotomy in bulbar poliomyelitis. About twenty-six papers on tracheotomy in bulbar poliomyelitis had been published since 1947, representing all shades of medical opinion. Some criticism was truly sharp; but it is of interest that the bitterest critics had not themselves used the method. However, the preponderance of opinion favored the method.

A large poliomyelitis epidemic in Denmark finally convinced the medical world that

tracheotomy could be a life-saving measure in respiratory obstruction arising from any part of the respiratory tract.

The tendency for more and more tracheotomies for respiratory emergencies other than the traditional one of laryngeal obstruction is well illustrated in the Table, made up from figures quoted by Nelson (1958).

Quoting Cawthorne further:

"The extended use of intratracheal anesthesia and in particular the use of closed-circuit machines made the anesthetists appreciate the potential danger of dead space air, particularly when the breathing was shallow. From this has come the realization that, in the shallow respiration of profound unconsciousness, the reduction of the dead space air from 150 cc. to 50 cc. by means of tracheostomy may in itself be life saving.

"Finally, the introduction by anesthetists of the cuffed intratracheal tube, which effectively isolates the lower respiratory tract from the digestive tract and at the same time allows for positive pressure respiration, has solved the problem of 'inhalation pneumonia' and has rendered the iron lung almost obsolete; and there can be few, if any, of those who have had to cope with patients in iron lungs who will regret this.

"The stimulus for this last step came from Denmark when, in 1952, they were struck by a serious epidemic of poliomyelitis with many cases of respiratory paralysis and not enough iron lungs to go around. They had to improvise and, by means of tracheostomy with cuffed tubes and by using teams of medical students to operate manually the positive pressure apparatus, many lives were saved. This led to the development of the mechanical positive pressure breathing machine."

Present Indications for Tracheotomy

Recently, trauma to the head, face, neck,

TABLE

	For Laryngeal Obstruction	For Other Causes Of Respiratory Insufficiency
1940	98%	2%
1954	53%	47%
1958	48%	52%

and chest has provided many indications for tracheotomy. Acute injuries of rather severe degree are becoming more common in our modern civilization with its rapid transportation.

Head Injuries

Tracheotomy is a useful procedure in head injuries with cerebral concussion, even though the face and neck are not injured. Pooling of secretion in the pharynx may occur, and aspiration of this secretion or of vomitus may follow. The use of tracheotomy to permit frequent and adequate cleansing of the lower respiratory tree has grown steadily in recent years.

Facial and Neck Trauma

Jaw fractures, injuries to the front of the neck with edema of the pharynx, and fracture and edema of the larynx make it necessary to provide an airway by opening the trachea below the point of injury.

Chest Injuries

During the past few years, the use of tracheotomy in the treatment of chest injuries has become more and more widespread. The purpose of tracheotomy in chest injury is twofold. Cleansing the lower respiratory tree by suction is probably the most important reason for doing tracheotomy in chest injuries. A second indication occurs in the so-called "flail chest." Here a large segment of the chest wall "floats," and there is paradoxical motion on respiration. When the patient breathes in, the flail segment of the chest goes in instead of out, because

it is no longer anchored to the rest of the chest wall. Positive pressure can be applied during the inspiratory phase of respiration to provide stabilization, or at least partial stabilization of the flail segment of the chest. This reduces pain and also increases respiratory efficiency.

Edema and Secretional Obstruction

Tracheotomy for relief of secretional obstruction in unconscious patients is not confined to head injury cases. It is useful in central nervous system vascular accidents, poisonings, botulism, and drug overdosage. Tracheotomy in burns may be necessary because of aspiration of hot gases which cause edema of the larynx. Of course, tracheotomy does nothing to overcome the primary disease *per se*; but it removes one deleterious factor from the patient's course and hence helps him to overcome the primary disease.

Conclusions

Tracheotomy was first performed in 1546 A.D., but until 1930 it was used only when suffocation from airway obstruction above or in the larynx existed. Then its value in overcoming secretional obstruction was recognized. Since then, its usefulness in bulbar poliomyelitis, head injury, burns, drug and microbial poisonings, chest injury, as well as in laryngeal and pharyngeal obstruction, has become apparent. The operation described by Fabricius of Aquapendente (1537-1619) as "the scandal of surgery" has now assumed a respected place in the surgeon's therapeutic arsenal.

Reference

1. Robert E. Priest, Tracheotomy: 124 B.C. to 1960 A.D., Presidential Address, Minnesota Academy of Medicine, Minnesota Med 43:813, 1960.

Reading maketh a Full Man; Conference a Ready Man; and Writing an Exact Man. And therefore, if a Man Write little, he had need have a Great Memory; if he Conferre little, he had need have a Present Wit; and if he Reade little, he had need have much Cunning, to seem to know that, he doth not. — Francis Bacon, Essayes

In political matters much may be said on both sides, and it always is.

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Foreign Body Problems

The Management of

PAUL G. BUNKER, M.D.*
Aberdeen, South Dakota

A COMPENDIUM on the subject, "Management of Foreign Body Problems," would be too exhaustive for this article; consequently it will be limited to those points of importance for the doctor who does not do endoscopy. These points are particularly important since foreign-body patients are usually seen first by the family physician, the pediatrician, or the internist. What these doctors *do* or *do not* do is often of life-saving importance in these emergencies.

Many deaths have resulted from unrecognized foreign bodies which are (unless an autopsy is done) usually attributed to coronary attacks. They occur most frequently in edentulous people who do or do not wear their dentures, especially when dining out, and often in combination with excessive drinking. Dr. Roger Haugen has coined the descriptive term "Cafe Coronary" for these cases.

Radiographic Studies

It is of the utmost importance that a foreign body be suspected in every unexplained respiratory difficulty or dysphagia. Adequate x-ray studies will usually establish the diagnosis, even with non-opaque foreign bodies. If a non-opaque foreign body is suspected in the air passages, inspiratory and expiratory films should always be made to show the changes typical of obstructive emphysema — including the hyperventilated lung and depressed diaphragm on the affected side, plus the mediastinal shift to the opposite side.

Complications

If the emphysema is not relieved by bronchoscopic removal of the foreign body, and if death has not ensued, atelectasis, either segmental or massive, will develop. Later, complications such as bronchiectasis, lung abscess, or even empyema can occur.

*Specialist in Otolaryngology and Bronchoesophagology.

If a foreign body is especially irritating, death can occur by a patient literally drowning in his own secretions. Death can also occur from a completely obstructing foreign body such as a large bolus of unchewed meat. A bean can quickly swell to approximately $2\frac{1}{2}$ times its normal size in the bronchial secretions and should be removed without delay. Similarly, a carrot can become macerated and softened into a complete plug. Peanuts may or may not provoke a fulminating reaction. Most peanuts are now eaten in a salted form which renders them less irritating.

Localization

Lateral x-rays should always be made to aid localizing an opaque foreign body. Such a body in the transverse position would be in the esophagus, whereas in the sagittal plane it would be in the larynx or trachea. Sometimes multiple coins will be directly superimposed in the action potential film and will appear as one, but can be clearly demonstrated in a true lateral view. In some cases it is necessary to x-ray all structures from the nasopharynx to the rectum to locate the foreign body. In children, x-rays should be made at $1/60$ of a second to eliminate motion. Do not be misled, however, if x-ray studies are negative.

Contrast Media

Contrast media are useful in locating a bone in the esophagus. My favorite method is to use a cotton pledget saturated in iodized oil. This will usually catch on the bone and, by providing bulk and lubrication, aid in spontaneous passage of the bone into the stomach. If this does not occur, the endoscopist can proceed immediately with the esophagoscopy, and the saturated pledget makes it easier to locate the foreign body. Barium, on the other hand, coats the esophageal wall and interferes with endoscopic visibility.

Symptoms

The most common symptom of a tracheo-bronchial foreign body is a wheeze. The rales are usually coarser and lack the sibilant

quality of a true asthmatic bronchitis. Children who are sick in bed with a respiratory infection or an asthmatic attack have time on their hands and are prone to put foreign bodies into their mouths. The overlapping of symptoms of an inhaled foreign body and the illness itself makes the diagnosis more difficult. A cough is also a common symptom of a foreign body, but the cough reflex fatigues rapidly; therefore the doctor should not be misled into a false sense of security when the cough subsides.

Pain and difficulty in swallowing plus excessive puddling of secretions in the hypopharynx and signs of infection are the most common symptoms of an esophageal foreign body.

Endoscopic Removal

In general, endoscopic removal is the only safe method for removing a foreign body from the esophagus or tracheobronchial tree. Meddlesome treatment is fraught with danger which can convert a simple foreign body into a difficult one, or result in serious complications. The latter occur most often with blind attempts at removal, especially trying to grasp the foreign body with a uterine forceps or to dislodge it with a stomach tube. Most foreign bodies lodge first in the larynx, setting up a violent spasm. If this is allowed to subside without interference, most of these foreign bodies will be coughed out.

Back-Slapping

At this stage, back-slapping will cause the patient to take a deep gasping breath, and the foreign body, if not coughed out, will more frequently be aspirated into the deeper air passages. Only if the patient is obviously dying, as manifested by continued choking and cyanosis, should back-slapping be attempted in a last desperate effort to induce the patient to cough the foreign body out.

Use of Fingers

Reaching into the mouth with a finger to remove a foreign body frequently converts a simple foreign body into a difficult one. When this is attempted the natural

reaction of an infant is to try to swallow the foreign body rather than to expectorate it. If the child is old enough to understand, encourage him to "spit" it out.

Esophageal Foreign Body

In adults with a bone in the esophagus, if the patient is not too uncomfortable, relaxants may be tried in the hope that the cricopharyngeal spasm will relax sufficiently to allow the bone to pass into the stomach. In this fortunate event, the patient should be put on a bulk producing diet and cautioned against taking any laxatives. Morphine still remains the best relaxant for this purpose.

Tracheotomy

A tracheotomy can be of life-saving importance if the foreign body is above the level of the tracheotomy opening. Indrawing of the suprasternal notch on inspiration would suggest this necessity. A large bolus of unchewed meat is the most common foreign body of this kind. Every physician should carry a razor-sharp knife for such an emergency. An emergency opening can be made through the cricothyroid membrane. Later a routine tracheotomy can be done if the need persists.

Proteolytic Enzymes

Proteolytic enzymes, where the foreign body is a large bolus of meat in the lower esophagus, can be useful if used judiciously. However, perforation of the esophagus with ensuing death has occurred from their use. In other patients a severe tracheobronchitis or bronchial pneumonia has occurred from aspiration of the highly irritating secretions resulting from their use. If the foreign body does not pass in four or five hours after giving them, esophagoscopy should be carried out without further delay.

Passage into Stomach

Most foreign bodies that pass into the stomach will pass along spontaneously, so that surgical interference is unnecessary. No laxatives should be given and the stools must be carefully examined for the foreign body. Radiopaque pointed foreign bodies should be followed by daily serial x-rays.

Occasionally a foreign body remains lodged in the fundus of the stomach for days or even weeks. To promote its passage into the intestines I give the child a bulky meal, then hold him up by the heels, thus utilizing gravity to get the foreign body out of the fundus into the main stream of gastric contents. While the child is still in this position, the parents are instructed to massage the abdomen with a pill-rolling motion to promote peristalsis, progressing in a circular manner around the entire abdomen. This is an old-fashioned treatment for atonic constipation. The patient is then placed on his right side for a period of 30 minutes to favor passage of the foreign body through the pylorus. This procedure is repeated after each meal.

Practical Points of Therapy

Do not be lulled into a false sense of security if the secondary infection responds to antibiotic therapy. If a foreign body is present, the infection will promptly return when treatment is discontinued.

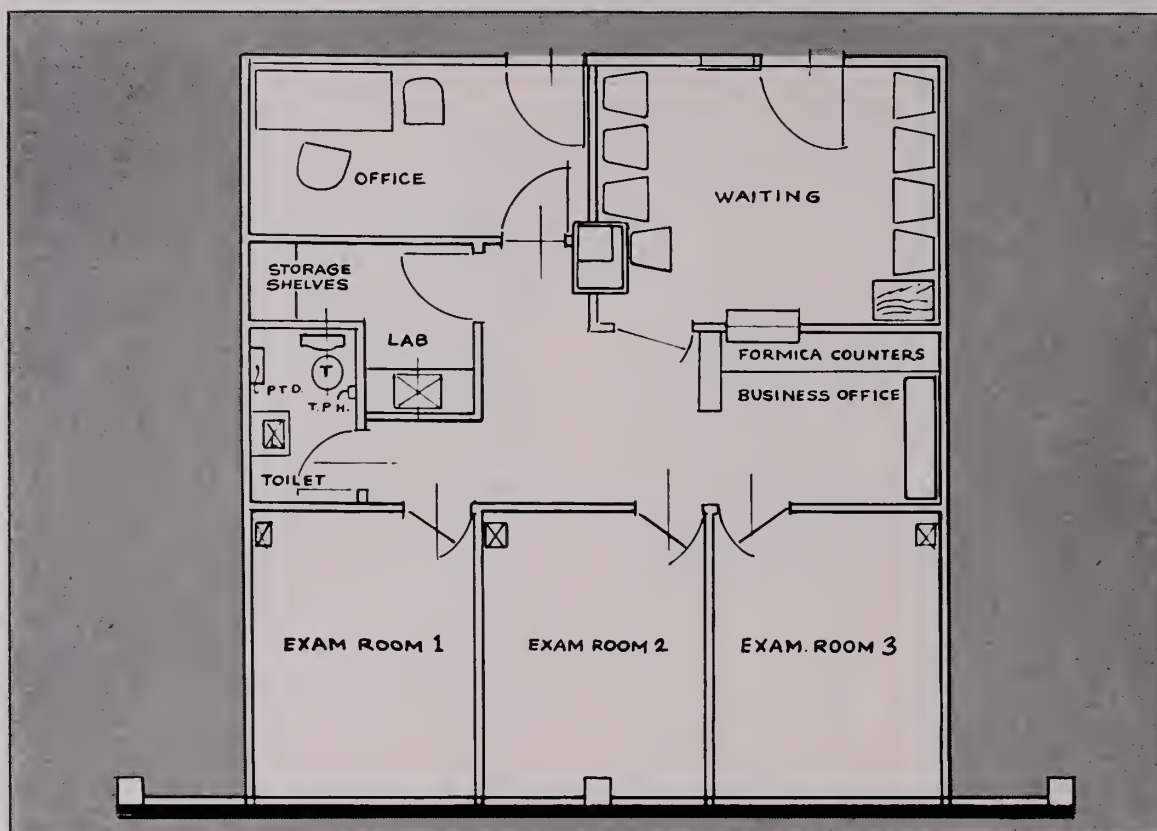
Try to send a duplicate of the foreign body with the patient so that the best forceps for grasping it can be pre-determined.

Never give dried bread or crackers to a foreign body patient. This stimulates gastric secretions which can greatly interfere with the esophagoscopy.

Respiratory depressants should never be given if there is marked difficulty in breathing. Death in these cases is usually from exhaustion, and the patients need to conserve all of their strength to continue breathing.

Obstinacy and heat in argument are surest proofs of folly. Is there anything so stubborn, obstinate, disdainful, contemplative, grave, serious, as an ass?

—Montaigne



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The Tonsil and Adenoid Problem

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IT IS INDEED ironic that there are no universally accepted indications for adenotonsillectomy — one of the most frequently performed operations in the United States. Approximately one third of the children in the United States have had adenotonsillectomies,¹ but over the last two decades there has been a gradual transition toward conservatism. This is in part a reaction to the previous philosophy that the presence of tonsils and adenoids constituted adequate justification for their removal. Unfortunately, some physicians have just as vehemently decried the procedure for any reason. As with most controversy, the “truth” is probably somewhere between the extremes.

Waldeyer's Ring is lymphoid tissue surrounding the entrance of the respiratory tract consisting of the adenoids (pharyngeal tonsil), the tonsils (palatine), and the lingual tonsils. In keeping with other lymphoid tissue, Waldeyer's Ring increases disproportionately in relative size early in life, coinciding with a period of many bacterial and viral upper respiratory infections. While it has been postulated that the lymphoid tissue of Waldeyer's Ring is important in the development of the immune process, recent thoughts are that any role it plays in the immune mechanism has ended at birth.

Because of the coexistence of frequent upper respiratory infections prior to age six years and large tonsils and adenoids, it has seemed a logical presumption that the large tonsils and adenoids were, at least in part, at fault. Occasional dramatic change in the upper respiratory infection pattern subsequent to adenotonsillectomy, but also at the time in life of natural decreased incidence, lent support to this hypothesis. Because the tonsils and adenoids are usually removed simultaneously, it has

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been difficult to assess the contribution, if any, of each procedure.

The Efficacy of Tonsillectomy

McKee² recently has conducted a rather well-controlled experiment into the efficacy of tonsillectomy. Excluded from this study were those patients for whom rather definite indications were present:

1. Peritonsillar abscess
2. Pyrexial tonsillitis accompanied by convulsions or flare-ups of renal or rheumatic disease.
3. Frequent or severe tonsillitis over a period of several years despite continuous antibiotic therapy.

Also excluded from the study by virtue of the fact that it was not considered adequate indication for tonsillectomy were those patients referred for colds, coughs, allergic symptoms and others who had had less than three episodes of probable throat infection with cervical adenitis within the preceding year. In addition, patients were excluded from the study if they were having their surgery for deafness, recurrent or chronic otitis media, or proven sinusitis. The patients selected for the McKee study were those whose symptoms indicated three or more isolated throat infections or acute respiratory infections with cervical adenitis within the previous twelve months. It was felt that in this group some physicians would recommend surgery while others would not. Patients were thereupon randomly allocated on the basis of their hospital number to immediate adenotonsillectomy or deferral for at least two years unless an urgent need subsequently presented itself.

Tonsillectomy

Analysis of these data showed quite well that the best results of the operation were in those patients under five years who had had three or more episodes in the preceding twelve months. By age eight years there was no evidence that tonsillectomy was of any value in reducing recurrent bouts of pharyngotonsillitis, unless there was significant morbidity for at least two years.

Adenotonsillectomy

A subsequent series³ comparing adenotonsillectomy with tonsillectomy alone demonstrated that adenoidectomy alone had no influence on the occurrence of throat disease, that otitis media occurred less frequently after either adenotonsillectomy or adenoidectomy, and that reduction of otitis media is attributable to the adenoidectomy rather than to the tonsillectomy. There were twice as many complications following the operation in the children having adenotonsillectomy as in those having adenoidectomy alone.

The logical conclusion therefore is that there are different indications for adenoidectomy than for tonsillectomy and that it may not be necessary or desirable to combine the two unless indications for each are present.

Adenoidectomy

If an adenoidectomy is indicated and the tonsils are left, what are the chances that a tonsillectomy will subsequently be indicated? An excellent study of this problem was carried out by Young⁴ who studied patients from six to nine years following adenoidectomy alone and found that in the entire series only one in eight subsequently developed an indication for tonsillectomy. Of those children over six who had indications for an adenoidectomy alone, only one in twenty subsequently developed indications for a tonsillectomy. It would seem therefore, unjustified to increase the morbidity and double the incidence of postoperative complications by doing an elective tonsillectomy, in the absence of indications, merely because the child is having an adenoidectomy.

Indications for Surgery

Bearing these findings in mind, the indications for surgery may be considered as follows:

Tonsillectomy

- A. Absolute
Peritonsillar abscess
- B. Relative

High Priority

Pyrexial tonsillitis accompanied by convulsions or flare-ups of renal or rheumatic disease.

Frequent and severe tonsillitis over a period of several years despite continuous antibiotic therapy.

Lesser priority

Three episodes of tonsillitis with cervical adenitis within the past twelve months for children seven or under and three or more bouts of tonsillitis with cervical adenitis per year for at least two years for those over seven years.

Removal of unusually large tonsils when necessary to facilitate an indicated adenoidectomy.

Adenoidectomy

- A. Recurrent acute suppurative otitis media.
- B. Recurrent middle ear effusion or secretory otitis media.
- C. Mouth breathing secondary to obstruction of the nasopharynx with adenoid tissue.

The Nature of Bacterial Invasion

One of the largest areas of confusion has been the differentiation of viral pharyngotonsillitis from bacterial pharyngotonsillitis. A recent study by Evans and Dick⁵ at the University of Wisconsin showed that for a college age population at least 26.3 percent were caused by hemolytic streptococci, 37.8

percent were caused by viruses, and 35.9 percent were of unknown etiology.

It is unfortunately very difficult without cultures to distinguish streptococcal from non-streptococcal infection in that an exudate was common to all of them. It was found, however, that there was a tendency for the white count to be generally higher in streptococcal infections and for the general malaise to be greater in viral infections.

Except for the absolute indication and a few of the high-priority indications for tonsillectomy, the morbidity of the procedure must be compared with the necessity of administering antibiotics for each subsequent bout of tonsillitis. For adenoidectomy, however, one must, in addition, consider the irreparable damage to the tympanic membrane, ossicular chain, and middle ear cavity if the eustachian tubes are blocked over a prolonged period of time or if recurrent bouts of otitis media are permitted.

In addition, prolonged mouth breathing from adenoid blockage of the choanae initiates a habit which is difficult to overcome later.

Conclusion

Adenoidectomy and tonsillectomy are two separate procedures with separate indications. They should be combined only when separate indications exist. Antibiotic therapy for recurrent tonsillitis can many times be substituted for tonsillectomy. Procrastination of an indicated adenoidectomy on the other hand may result in irreparable damage to the patient's hearing.

References

1. Caplan, A.: A Review of the Tonsil and Adenoid Problem. *Manitoba Med Rev* 44:470, 1964.
2. McKee, W. J. E.: A Controlled Study of the Effects of Tonsillectomy and Adenoidectomy in Children. *Brit J Prev Soc Med* 17:49, 1963.
3. McKee, W. J. E.: The Part Played by Adenoidectomy in the Combined Operation of Tonsillectomy and Adenoidectomy. *Brit J Prev Soc Med* 17:133, 1963.
4. Young, I. S.: Adenoidectomy: How Often is Tonsillectomy Necessary Later? *J Laryng* 76:791, 1962.
5. Evans, A. C. and Dick, E. C.: Acute Pharyngitis and Tonsillitis in University of Wisconsin Students. *JAMA* 190:699, 1964.

Pliny on Corns

Whoever, when he sees a shooting-star, soon afterward pours a little vinegar upon the hinge of a door, is sure to get rid of his corns.

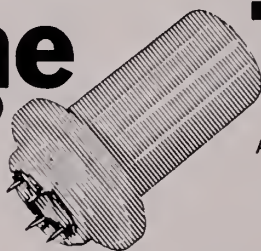
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Disease of the Major Salivary Glands

Classification, Diagnosis and Treatment

THE MAJOR SALIVARY glands can be affected by many pathological disorders. One or more glands may be affected. Primary disease is common. Less common is involvement by encroachment, metastases and local manifestations of constitutional disease. The following broad classifications of diseases must be considered:

1. Inflammatory
2. Endocrine and metabolic
3. Neoplastic
4. Traumatic
5. Cystic

Diagnosis

In order to assist the physician in arriving at a judgment upon which rational and definitive therapy can be based, the following diagnostic procedures are available: history and physical examination, general laboratory studies, salivary cytological studies, smears and cultures, sialometry, roentgenographic studies including sialography, duct probing and cannulization, incisional and excisional biopsy and microscopic tissue examination, and finally, where diagnosis still remains obscure, the patient must be periodically re-examined and re-evaluated.

Inflammatory Disorders

Acute

A common acute inflammatory disease involving one or more major salivary glands is mumps (epidemic parotitis). Another is acute sialdochitis, which can be of viral or bacterial origin. Acute sialadenitis is usually self-limited but can lead to abscess formation. Coalescence is usually slow to develop in the parotid gland due to the dense fascial septa. Sialadenitis from an allergic or drug reaction is frequently multiglandular.

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Chronic

Chronic inflammatory disease can conveniently be classified as recurrent or progressive. Chronic recurrent disease includes: recurrent sialadenitis, sialectasis, sialolithiasis and duct or orifice stricture. It is not uncommon for patients with chronic recurrent disorders to have acute exacerbations. Commonly pyogenic bacteria are the organisms which account for the exacerbations and chronicity. If the condition progresses, fibrosis and lymphocytic infiltration develop.

Later, destruction of the ductal and secreting elements of the gland occurs. Chronic progressive disease results from granulomatous lesions, such as tuberculosis, sarcoidosis, mycosis infections and benign lymphoepithelial disease (Mikulicz's disease and Sjogren's syndrome).

Treatment

The treatment of patients with salivary gland disease of inflammatory origin can be medical or surgical or a combination of both. Thus the treatment may vary from conservative medical treatment in patients with mumps to other patients with inflammatory diseases, who might require duct probing, removal of stones and strictures or wide surgical incision or excision. Radiation therapy may be used judiciously, particularly in those patients with early acute sialadenitis.

Metabolic and Endocrine Disorders

The disorders which result from endocrine and metabolic disturbances are usually manifested by hypertrophy, enlargement and change of consistency of the affected gland. One or both parotid glands are involved more frequently than the submandibular or sublingual glands.

Hypertrophy

Benign hypertrophy can occur in patients with thyroid gland dysfunction, in the diabetic, or in some patients with alteration of pituitary-adrenal axis.

Atrophy

On the other hand, benign atrophy of

glandular structures can occur associated with fatty or fibrous atrophy. In these disorders, the parotid glands appear to enlarge. Even though the glandular elements progressively atrophy, replacement by fatty or fibrous tissues accounts for the enlargement.

The parotid gland atrophies are without symptoms and occur in patients with a wide variety of conditions, varying from exogenous obesity to collagen diseases. Menopausal hypertrophies are manifested mostly in the parotid glands. Likewise, in some deficiency states, hypertrophy can occur.

In these patients, treatment is symptomatic and directed for the most part to the constitutional endocrine or metabolic disorder. Rarely is biopsy indicated.

Neoplastic Disorders

Neoplasia of the major salivary glands can be benign or malignant and of fibrous or epithelial tissue origin. Further, neoplasias can be a manifestation of constitutional or metastatic disease and, finally, they can occur as direct encroachment from adjacent neoplastic disease.

Benign Mixed Tumors

In the parotid glands the benign mixed tumors are most common, being present in 60-65% of the cases of primary tumors. They occur with less frequency in the submandibular glands. The prognosis is much more favorable in patients with primary malignancies of the parotid glands than in patients with primary malignancies of the submandibular glands.

Diagnosis

Sialography can be misleading and must be used judiciously in tumor diagnosis. In patients with suspected, highly malignant lesions (primary or otherwise) incisional biopsy may be permitted. As a rule, however, wide surgical excision is the treatment of choice. The facial nerve is preserved whenever feasible. If, by necessity, for acceptable excisional removal of the tumor, the facial nerve must be removed, then suture or grafting should be done, either

as a primary or secondary surgical procedure.

Frozen Section

The surgeon and the pathologist must both be continually cautious of final diagnosis by microscopic examination of tissues prepared by frozen section techniques. It may be more feasible for the surgeon to delay destructive surgery in these patients until permanent tissue sections can be prepared.

"Unclassified Tumors"

In recent years the tumors of the major salivary glands are better understood and the group of so-called "unclassified tumors" is smaller. The cooperative efforts of the surgeon, pathologist, radiologist and internist have all accounted for this by astute clinical diagnosis, by improved surgery and radiation therapy, and by follow-up examinations extending over many years.

Surgical Considerations

In most instances, the benign tumor of fibrous tissue origin should be excised widely. In the parotid gland the facial nerve must be preserved. Patients with primary lymphangiomas, lipomas and neuromas, fall into this category. On the other hand, infants with hemangiomas should be observed for expected disappearance. If the hemangioma enlarges or persists, then surgery is indicated.

Since the malignant tumors of fibrous or supporting tissue origin occur often as a local manifestation of constitutional disease, treatment is often medical in the form of chemotherapy or radiation therapy. In some patients with localized malignancy surgery may be carried out. The facial nerve is usually excised and may or may not be sutured or grafted.

Benign Epithelial Tumors

Benign tumors of epithelial origin occur as the benign mixed, mucoepidermoid "tumors" or adenomas. The benign mixed account for 65% of the primary parotid gland tumors. There are stromal and epithelial varieties. They occur in any portion of the parotid gland and may be

deep or superficial to the facial nerve. Medial extensions of the tumor from the retro-mandibular portion of the parotid or from the tail can enter the parapharyngeal space.

Parotidectomy

In any event, the treatment of choice is parotidectomy with preservation of the facial nerve. Recurrence as a rule is due to inadequate surgery. Patients with benign mixed tumors of the submandibular gland are candidates for surgical excision. Total parotidectomy should be done in patients with mucoepidermoid "tumors."

It is often difficult for the surgeon and the pathologist to determine benignity from either microscopic frozen or permanent tissue examinations. Hence radical surgery is indicated with preservation of the facial nerve. Follow-up examination is most important. Benign adenomas should be excised without facial nerve injury. These lesions include papillary lymphoid cystadenomas (Wharthin's tumor), the acidophilic cell and the serous cell adenomas.

Malignant Epithelial Tumors

Malignant tumors of epithelial primary origin in the parotid gland account for 20-25% of tumors and 30-40% of malignancies in the submandibular glands. Malignancies of the submandibular glands have a poorer prognosis than those of the parotid glands. Primary squamous cell carcinomas may be cornifying, non-cornifying or lymphoepithelial in character.

Treatment

Incisional biopsy may be permitted in some of these patients. Radiation therapy can be the treatment of choice, or it may be indicated following surgical excision. The surgeon must decide whether or not the facial nerve is to be removed. Nerve suture or graft is not contraindicated, even though postsurgical radiation therapy is used. In continuity, block dissection of the neck should be done in patients with neck node metastases. Neck dissection may be indicated as a later operation in other patients.

Patients with malignant tumors of gland

cell origin are often difficult to treat. Surgery varies from excisional parotidectomy with facial nerve preservation to radical excision of the gland with neck dissection, removal of the pinna and partial excision of the temporal bone, hemimandibulectomy and VIIth nerve removal. Radiation therapy is recommended as a follow-up form of post-surgery therapy in some patients.

The capricious nature and the clinical behavior of most of these tumors require years of patient follow-up. At follow-up examinations, the patient must be checked for local recurrence, as well as for metastatic disease.

This group includes patients with adenoid cystic adenocarcinomas, serous cell adenocarcinomas and acidophilic adenocarcinomas. Patients with malignant mucoepidermoid "tumors" require radical excision. Perhaps the group of patients with "unclassified" malignant epithelial gland cell tumors present more problems in diagnosis and treatment for the surgeon, pathologist and radiotherapist than do patients with any other malignancies. This is because these tumors often behave in bizarre fashion.

Traumatic Disorders

The parotid gland may be involved in crushing, lacerating, penetrating or other forms of injury.

Facial Nerve

If injury is recent, it may be the opportune time to repair the facial nerve when severed. The facial nerve electrical stimulator can be used to identify peripheral cut fibers up to three days post injury. The proximal cut ends are identified less readily. Main trunk identification away from the laceration and peripheral dissection may be the surgeon's choice to identify the proximal stumps.

In other patients, the surgeon may iden-

tify a proximal cut stump and trace this posteriorly to the pes annerimus. In this manner, other cut branches may be identified by tracing them distally through the parotid gland.

Serious Injury

In seriously injured patients, choice of priority of treatment often modifies timing of parotid gland and facial nerve repair. If Stensen's duct is lacerated, it should be sutured over a polyethylene tube, anchored with a "stay" suture at the papilla in the buccal cavity. In the surgical exploration of patients with parotid gland injuries, bone fractures must be noted and treated. Likewise, the soft tissues must be debrided, foreign bodies removed and the soft tissues meticulously approximated by suture. If significant trauma occurs to the submandibular gland, it should be removed. Injury occurs less frequently here than in the parotid glands because of the protection of the horizontal ramus of the mandible. Nerve suture or graft of the mandibular division of the facial nerve can be accomplished in some patients. If severed, the lingual nerve should also be sutured.

Cystic Disorders

Cysts of the major salivary glands can follow trauma, stricture, inflammation; or they may occur as a congenital lesion. The parotid gland is most frequently affected. When patients have symptomatic disease, treatment is surgical. In the parotid gland this may mean total parotidectomy with preservation of the facial nerve. This is particularly true when the cysts are multilocular and extensive. In some patients with superimposed, acute inflammation, external incision and drainage should be carried out, followed by wide surgical excision as a secondary procedure when indicated.

Individualism

It would seem that the study of medicine does not always contribute to broadmindedness, as men who choose medicine as a profession are apt to lose rather than gain breadth of perception. It could be said rather that medicine develops individualism.

— Charles Mayo

A Mass in the Neck

The Diagnostic Approach

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THE DIAGNOSIS OF masses in the neck has been the subject of innumerable articles in medical literature. The manifold interest in masses in this portion of the body is easily understood when one recognizes the complexity of highly important structures in this region, the many and varied types of tissue present, and the many opportunities for congenital abnormalities to occur in this area. It is the purpose of this presentation to evaluate the important, present-day, common diagnostic problems relating to neck masses as they affect the lives of the majority of patients encountered with such masses, rather than to recount a complete differential diagnosis.

Midline Neck Masses

With the reader's understanding that this is not an attempt to explore and discuss all causes of neck masses, it is possible to divide them into two main categories; midline and lateral. It is then possible to fairly quickly dispense with midline masses, since these are by and large of thyroid origin, well-known to most physicians and quite easily diagnosed as enlargements of the thyroid lobe, the thyroid isthmus, or developmental abnormalities of thyroid development such as midline aberrant thyroid, thyroglossal duct cyst, etc. With the exception of dermoid cysts, which may appear in or near the midline of the neck, such thyroid abnormalities constitute by far the huge majority of midline masses and present no significant problem of diagnosis.

Lateral Neck Masses

The remaining cervical swellings of diagnostic import are, therefore, composed of the masses appearing in the lateral portion of the neck, the largest number of which (excluding infectious lymphadenitis in chil-

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dren) constitute metastatic foci from primary malignancies elsewhere in the body. Again, by far the greatest percentage of such metastases is from the area of the head and neck, albeit cervical metastatic nodes may occasionally appear from other primary sources such as the lungs, stomach, pancreas, etc. It should be realized that approximately 80% of lateral neck masses constitute metastatic neoplastic disease, mainly from primaries in the head and neck region.

Benign Lesions

Accordingly, it is important that the primary attention and thinking of the examining physician be centered about this possibility, rather than the rare or esoteric causes of lateral cervical swelling such as branchial cleft cysts, laryngoceles, pharyngeal and esophageal diverticuli, dermoid cysts, sebaceous cysts, cystic hygroma, submaxillary gland enlargement due to ductal obstruction, etc.

Fortunately, these more rare causes of neck masses are accompanied by a history of longer duration, cystic nature on examination, or such other unusual signs and symptoms as to allow the luxury of leisurely study and contemplation of their etiology prior to definitive diagnosis.

Diagnostic Approach

The presence of a firm swelling in the lateral portion of the neck must be considered malignant until proven otherwise. Its nature and origin demand a speedy and definitive diagnosis to insure prompt and proper therapy. All too often the patient's life is dependent upon proper and expeditious evaluation of the cervical mass.

Search for Primary First

One of the most serious mistakes that can be made in diagnosing a mass in the neck is that of proceeding directly to open biopsy. Otolaryngologists and other head and neck surgeons are continually faced with the surgical problems and dire consequences of neck biopsy without a thorough and complete search of the upper respiratory tract for evidence of a primary source of malignancy.

All too often, biopsy of a cervical node is considered the most direct approach to a diagnosis, or a thorough search for a primary site is neglected because of the examiner's inability to adequately examine the many areas wherein a primary carcinoma may lurk.

This is to be decried, since the proper management of most carcinomas of the head and neck, with cervical metastases, entails an en-bloc resection of the primary with a radical neck dissection encompassing the connecting lymphatics in one specimen.

Problems of Open Biopsy

Prior biopsy of the neck metastasis greatly compromises the patient's chance of cure by seeding of the surrounding tissues and by opening lymphatics for further spread of cancer cells. Accordingly, it can be categorically stated that, rather than being the most direct approach for the establishment of diagnosis of a lateral cervical mass, open biopsy should be reserved as the *last* diagnostic procedure in such swellings.

It must be remembered that if a thorough search for a primary source of malignancy does reveal a primary lesion, the preliminary biopsy of cervical nodes not only increases the chances of dissemination of disease in the neck but limits the benefits of neck dissection. Likewise, it makes the resulting neck surgery infinitely more difficult because of biopsy scarring and the necessity of including large areas of skin and subcutaneous tissues in the operative specimen.

Upper Respiratory Tract

From the above considerations it is readily seen that the most important diagnostic measure in the evaluation of a cervical neck mass is that of a complete and thorough examination of the upper respiratory tract in the search for a primary carcinoma.

Nose and Nasopharynx

This search must include a minute examination of the nasopharynx with both the nasopharyngeal mirror and nasopharyngoscope, since lesions in this area are notor-

iously treacherous and may appear as only slight fullnesses of the submucosal tissues or as slight fissures in the nasopharyngeal mucosa. The entire area of the pharynx, mouth, tongue, and floor of the mouth must be examined very carefully, not only by direct visualization, but also by palpation, to detect the firm, deep lesion which may be present within the substance of the tongue or tonsillar tissue, escaping the notice of surface examination.

The interior of the nose must be searched with the nasal speculum and nasopharyngoscope after the mucosa has been satisfactorily shrunk with topical vasoconstrictors. The search for an obscure primary lesion should also involve diagnostic radiographic studies of the sinuses.

Larynx and Hypopharynx

The larynx and hypopharynx must be explored by indirect laryngoscopy with adequate topical anesthesia so that all areas of the larynx, hypopharynx, and pyriform sinuses are satisfactorily visualized. If any of these laryngopharyngeal areas are not completely visualized, the patient should have a direct laryngoscopy before the search is considered complete. Only after such a survey of the upper respiratory tract has been completed, is biopsy of the cervical mass justified.

Needle Biopsy

In the instance where no primary lesion has been found and good pathology facilities are available, it is the author's opinion that needle biopsy is preferable to open biopsy. In the event that the cervical mass is cystic rather than metastatic, this will be elucidated by needle biopsy; and if a mass does represent metastatic carcinoma, this may be verified by needle biopsy with minimal dissemination of tumor cells and the least compromise of subsequent therapy by surgery or radiotherapy.

Open Biopsy

If needle biopsy is inconclusive or if pathology facilities are unavailable for reliable interpretation of needle biopsy mater-

ial, then and only then is open biopsy of cervical masses indicated. When open biopsy is utilized, it should be done through a minimal incision placed within the prospective incision lines of a subsequent radical neck dissection if this becomes necessary.

If a large solid tumor is encountered, biopsy specimens only should be obtained, to minimize the deleterious effect upon a subsequent neck dissection, rather than attempting to remove the mass by local excision. On the other hand, if small lymph nodes are encountered, it is preferable to remove an entire node for biopsy rather than violate its capsule. If a cystic or otherwise obviously benign condition is encountered at the time of biopsy, then of course the operative site can be extended and the lesion removed as definitive treatment.

Frozen Section

In the absence of a known or suspected primary lesion, the reliance on frozen section biopsy in the decision to proceed with radical neck dissection is ill-advised. Permanent sections might indicate lymphoma or other pathology wherein further surgery would be detrimental or might give a clue to repeat a search for a primary locus wherein an en-bloc resection, with the primary, would be of much more benefit than separate resection.

Radical Neck Dissection

In the instance where the patient has had a previously known and treated primary carcinoma in the region of the head and neck, a cervical mass should be approached vigorously. No more than two to three weeks time should be utilized in hoping that the cervical mass is inflammatory. It has been demonstrated that approximately 80% of such cervical nodes in the drainage field of previous head and neck malignancies are, indeed, metastatic.

With this type of odds, one is well justified to proceed with definitive radical neck dissection in the attempt to achieve a maximal chance of cure, rather than be party to further delay or other diagnostic measures. If one feels that there is serious doubt and

wishes to have the support of biopsy confirmation, such biopsy should be done in the operating room with frozen section and preparation to proceed immediately with radical neck dissection. The specimen in this case should include the skin and subcutaneous tissues violated by the biopsy procedure.

Summary

A practical consideration of the diagnosis of masses in the neck indicates that, in adults, such masses usually fall into the category of easily diagnosable midline swellings of thyroid nature or occur in the lateral portions of the neck. Approximately 80% of lateral cervical masses represent metastatic malignancy and, therefore, must

be viewed with alarm and evaluated without undue delay.

Proper evaluation of lateral cervical masses must begin with, and include, a careful and complete examination to detect the slightest aberration indicative of a possible primary malignancy.

Open biopsy is the *last* diagnostic measure to be employed in the evaluation of a cervical mass and must be performed by a surgeon prepared to proceed with definitive removal of a benign lesion if encountered, and with a full understanding and respect for the influence and effect of such biopsy on subsequent total management of the disease process, if the mass be of a malignant nature.

On Diet and Hygiene From Regimen Sanitatis Salernitanum

Eggs newly laid and broths of richest juice
 With ruby wine, increase of strength produce,
 Wheat and milk make flesh, brains and tender cheese,
 Marrow and pork as taste they chance to please.
 Or eggs with art prepared, or honeyed wine;
 Ripe figs and grapes gathered from the vine.

Let air you breathe be sunny, clear and light,
 Free from disease, or cesspool's fetid blight.

From washing after meals two gains arise:
 The hands are cleansed and strengthened are the eyes.
 If thou in health prolonged wouldst ever stay,
 Wash frequently thy hands each passing day.

Goat's milk and camel's, as by all is known,
 Relieve poor mortals in consumption thrown;
 While asses' milk is deemed far more nutritious,
 And e'en beyond all cow's or sheep's officious.
 But should a fever in the system riot,
 Or headache, let the patient shun the diet.

Neurosis does not deny the existence of reality, it merely tries to ignore it: psychosis denies it and tries to substitute something else for it. A reaction which combines features of both these is one we call normal or "healthy"; it denies reality as little as neurosis, but then, like a psychosis, is concerned with effecting a change in it.

— Freud

Make me chaste and continent, but not just yet. — Saint Augustine

Palatal Insufficiency

Correction of

DEAN M. LIERLE, M.D.*
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Iowa City, Iowa

VELOPHARYNGEAL INCOMPETENCE, the inability of a person to speak without noticeable nasality, can result from a variety of conditions. Whatever the etiology the mechanism is essentially the same: inability to close the port between the mouth and the nose. This is true whether the nasality is due to palatal excision for malignancy, paralysis, congenital shortness, cerebral palsy, scarring or cleft palate. The last named condition is by far the most common etiologic factor and further discussion will be limited to it.

Nearly every aspect of cleft palate management is a matter of some controversy. Included in the moot points are the method of management (prosthetic or surgical?), the age at which any contemplated primary surgery should be done, type of surgical repair, efficacy of any type of treatment, need and desirability of secondary surgical procedures and so ad infinitum.

The Use of Prostheses

Except in instances presenting some definite contraindication, most people concerned with palatal clefts prefer surgical repair to prostheses. These dental appliances need to be removed and cleaned several times a day, must be changed in size to keep pace with a child's growth, are subject to breakage, and are certainly of no benefit to the teeth to which they must be attached. However, when definitive surgery cannot be done or when it has failed, prosthetic obturation can be a great boon.¹

Surgical Repair

Surgical repair of a cleft palate is like any other type of surgery in that it does not always produce the desired result, elimination of hypernasality in speech. This is most often due to the fact that so many cleft palates are not only split palates but,

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in addition, are shorter than the non-cleft palate. After repair of the cleft the posterior edge of the short palate is unable to contact the posterior pharyngeal wall when needed in the speech process, and thus permits nasal escape of air. Unfortunate patients who cannot gain velopharyngeal competence after repair of a palate may receive great improvement through intensive speech training by a competent clinician. In many communities a speech clinician is an integral part of the public school system.

There remains a large percentage of cleft palate patients who have hypernasal speech after palate repair and competent speech therapy. There are also many postoperative individuals who have overcome this palatal insufficiency only by developing nares constriction and other facial grimaces. All of these are candidates for further physical management, and again we encounter disagreement in the choice of therapy. Some will be helped a great deal by a dental appliance that lifts the soft palate a few millimeters. Others achieve acceptable speech by resorting to an obturator, an appliance that has a bulb attached to a palatal portion posteriorly and is designed to decrease the size of the port between the oropharynx and the nasopharynx.

Secondary surgical procedures aimed at obviating hypernasal speech are legion and nearly everyone of them has its ardent admirers and bitter detractors. Should the palate be lengthened by one or more of several operations devised for the situation?² Should the posterior pharyngeal wall be brought forward by a reefing procedure³ or by submucosal implantation of a graft?^{4,5} Should the size of the aperture between the soft palate and posterior pharyngeal wall be decreased by lifting a flap from the pharyngeal wall and attaching it to part of the width of the free edge of the soft palate?⁶ Should the flap be lifted and rolled up into a ball without attaching it to the soft palate?⁷

At this point it might be wise to digress from secondary velopharyngeal surgical procedures and return for a short time to a few more considerations concerning primary

palatal repair. There are surgeons who practically never repair a cleft palate without incorporating a lengthening procedure.^{2,11,12} There are some who include the attachment of a pharyngeal flap to the posterior edge of the palate as part of a first operation in order to reduce the number of patients who have poor speech after palatal repair.⁸ Quite a few otologists decry the latter concept as it closes access to the nasopharynx for treatment to alleviate ear disease without detaching the flap.

The Lengthening Procedure

One might well ask why the lengthening procedure and, particularly, the flap attachment should be included in the primary operation only in instances where palatal repair was not expected to produce the desired speech result. The answer is an embarrassing one for all concerned. Most people agree that the prognosis concerning speech before or during palatal repair is almost wholly a matter of conjecture.

The original types of lengthening procedures gave poor results in the hands of many surgeons. This was probably due to the fact that a raw surface was left on the mucoperiosteal flap that was moved backward from the hard palate.⁹ Because the raw area had to heal by secondary intention and scar contraction the palate could not maintain its retroplacement. After this was realized, efforts were made to avoid it by placing a skin graft on the raw surface of the flap.¹⁰ This maneuver prevented contracture and reshortening to some degree but often added another objectionable feature, a foul breath resulting from retained desquamated epithelium on the graft's surface. Recent attempts to avoid these two unhappy results have included posterior movement of mucosa from the floor of the nasal cavity¹¹ or fashioning a turnover flap of palatal mucoperiosteum based on one or both greater palatine neurovascular bundles.¹²

Parents of children with repaired cleft palates and adults who suffer from palatal insufficiency are not often aware that further physical management may offer aston-

ishing speech improvement. Due to this paucity of information among the population with palatal incompetence and among persons who might impart information to them, quite a few cleft palate services hold annual information seminars for physicians, dentists, public school personnel, social workers and speech pathologists.

Discussion

The confusion evident in this presentation is no greater than that which exists among persons who are intimately associated with the management of palatal insufficiency. However, by whatever methods happen to be employed by an individual or institution, a great percentage of persons with velopharyngeal incompetence can achieve socially acceptable speech. It is therefore the responsibility of all the allied professions to pursue the problem to the ultimate attainment of all possible improvement in communicative ability.

Results

Analysis of 123 pharyngeal flap procedures done between 1955 and 1962 revealed

that 83.3% had attained velopharyngeal competence.¹³ An additional 100 patients who have had pharyngeal flaps continue to support this degree of palatal improvement.

The success of the operation appears to depend on the width of the flap and the amount of preoperative movement of the palate and lateral pharyngeal walls. Satisfactory results are less frequent in patients over 15 years of age and in those with defective intelligence. It is usually contraindicated in individuals with chronic middle ear disease, chronic sinusitis, or allergic rhinitis.¹⁴

There are a few complications; among these are hemorrhage, partial or total loss of the flap, atresia, and airway obstruction in young children due to pharyngeal edema.

Conclusions

The only valid assessment of the success of pharyngeal flap procedures involves evaluation of the postoperative potential for velopharyngeal closure. This can be observed in nearly all the cases. Speech status evaluations are relevant only to the degree to which they reflect the potential closure.¹³

References

1. Olin, W. H.: Cleft Lip and Palate Rehabilitation. p. 134, Charles Thomas, Springfield, Ill., 1960.
2. Steffensen, W. H.: Palate Lengthening Operations *Plast Reconstr Surg* 10:380, 1952.
3. Wardill, W. E. M.: Cleft Palate. *Brit J Surg* 16:127, 1928.
4. Blocksma, R.: Correction of Velopharyngeal Insufficiency by Silastic Pharyngeal Implant. *Plast Reconstr Surg* 31:268, 1963.
5. Hagerty, R. F., and Hill, M. J.: Cartilage Pharyngoplasty in Cleft Palate Patients. *Surg Gynec Obstet* 112:350, 1961.
6. Conway, H., and Goulian, D.: Experiences with the Pharyngeal Flap in Cleft Palate Surgery. *Plast Reconstr Surg* 26:590, 1960.
7. Barsky, A. J., Kahn, S., and Simon, B. E.: Principles and Practice of Plastic Surgery (2nd Ed.) p. 393, McGraw-Hill Book Co., New York, Toronto, London, 1964.
8. Webster, R. C., Quigley, L. F., Coffey, R. J., Querze, R. H., and Russell, T. A.: Pharyngeal Flap Staphylorrhaphy and Speech Aid as a Means of Avoiding Maxillofacial Growth Abnormalities in Patients with Cleft Palate. *Amer J Surg* 96: 820, 1958.
9. Dorrance, G. M.: Lengthening the Soft Palate in Cleft Palate Operations. *Ann Surg* 82:208, 1925.
10. Dorrance, G. M., and Bronsfield, J. W.: Cleft Palate. *Ann Surg* 117:1, 1943.
11. Brauer, R. O.: Push-back Repair of the Cleft Palate with Nasal Mucosal Flaps to Prevent Late Contracture. *Plast Reconstr Surg* 36:529, 1965.
12. Millard, D. R.: The Island Flap in Cleft Palate Surgery. *Surg Gynec Obstet* 116:297, 1963.
13. Smith, J. K., Huffman, W. C., Lierle, D. M., and Moll, K. L.: Results of Pharyngeal Flap Surgery in Patients with Velopharyngeal Incompetence. *Plast Reconstr Surg* 32:493, 1963.
14. Moll, K. L., Huffman, W. C., Lierle, D. M., and Smith, J. K.: Factors Related to the Success of Pharyngeal Flap Procedures. *Plast Reconstr Surg* 32:581, 1963.

Derivately Speaking

Phthisis — from Greek *phthiein* (to decay).

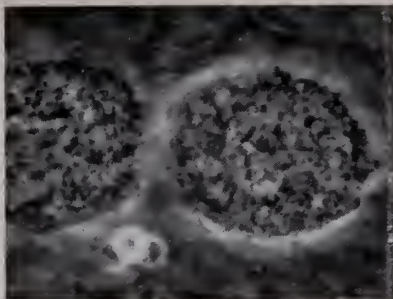
INFLAMMATION: A cellular fight for life

A SYNTEX REPORT based on recently developed hypotheses about topical corticosteroids, including the cellular theories of inflammation by Thomas F. Dougherty, Ph.D., University of Utah.

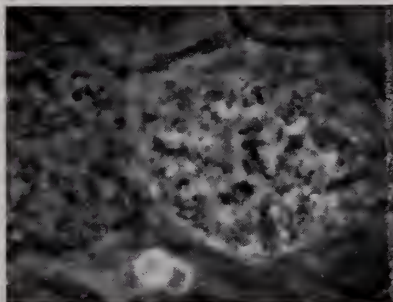
You are looking at a fibroblast fighting for life. This cell—one of the most common found in connective tissue—has literally been poisoned by cytotoxins released from other cells that have ruptured. Soon, if the abnormal activity of this fibroblast does not cease, it, too, will rupture and die—one more casualty in the inflammatory wave of destruction precipitated by injury.

Until a short time ago no one had ever witnessed such a scene at the cellular level. Now, through advanced cinemicrographic techniques, it is possible to view and photograph the inflammatory process as produced experimentally in living animal tissue. This method permits new insight into the mechanism of inflammation and the role of corticosteroids in therapeutic management. Equally important, these techniques shed new light on factors that may make one corticosteroid more effective than another—factors that can be correlated with other chemical, biologic, and clinical parameters.





Phase-contrast microscopy showing mast cell before injury.



Mast cell (after injury) has broken up and released cytotoxins.

Visual evidence of how corticosteroids influence the inflammatory reaction

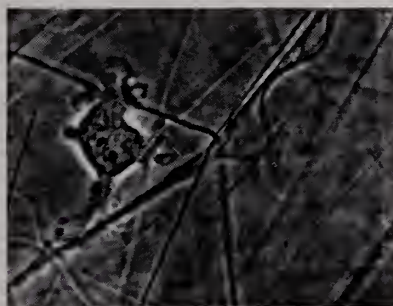
Working with phase-contrast cine-micrography on living animal tissue, Doctors Thomas F. Dougherty and David Berliner of the University of Utah College of Medicine have actually filmed cellular events that occur during the inflammatory reaction. This remarkable study* and additional work by these investigators, as well as by others, have established a new theoretical biologic basis for the antiinflammatory effect of the corticosteroids. (It must be noted that other theories, such as the lysosome or so-called "suicide bag" theory, have been postulated, although it is quite likely that there are more similarities than differences among the various theoretical models.)

The inflammatory wave of destruction

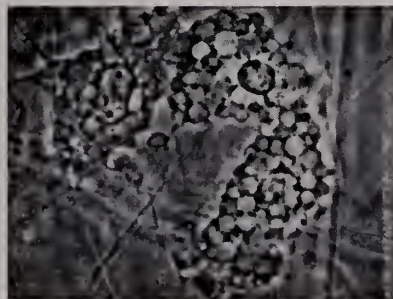
In this investigation an injurious injection of gelatin is used to set off an inflammatory reaction in living mouse tissue. What follows is a wave of destructive cellular activity that comprises the inflammatory response to injury. Mast cells (which contain heparin, serotonin and histamine) take up water, swell and rupture, releasing their contents, which are toxic outside the mast cell wall. These toxins, in turn, cause disintegration of other cells (such as fibroblasts) and the release of additional toxic material. Capillaries, too, take up water and leak unformed blood elements, causing edema. And polymorphonuclears, lymphocytes and perithelial cells invade the inflamed site. As a result of all these changes, the cellular environment reaches a state of turmoil.

How corticosteroids change the picture

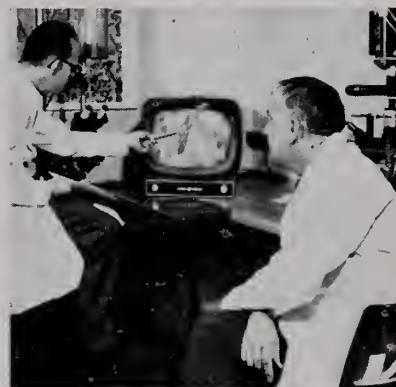
Corticosteroids appear to virtually stop the abnormal cellular activity that constitutes the inflammatory reaction. This permits the body's natural resources to clear up the inflamed area and repair the damaged tissue. This interpretation is supported by the fact that when the injurious gelatin solution is injected simultaneously with a corticosteroid — Synalar (fluocinolone acetonide) — the inflammatory pattern simply does not develop.



Fibroblast in high state of activity, much distorted.



Mast cells showing effects of corticosteroid action: cells are normal in size, shape and activity.

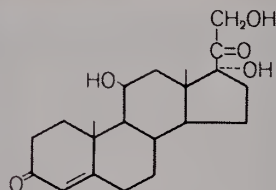


In summarizing his study Doctor Dougherty states: "...we also feel this work may explain why one corticosteroid helps a patient more rapidly and effectively than another. If it does, it is because one corticosteroid is the fastest, most effective inhibitor of the series of inflammatory events at the tissue level."

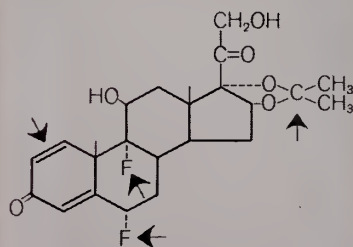
*A New View of Corticosteroid Action in Inflammatory Dermatoses, a film based on this study, is now available from your Syntex representative.

How advances in chemical design have achieved greater steroid potency

The chemical modification of corticosteroid molecules from the advent of hydrocortisone to the development of Synalar (fluocinolone acetonide) is a prime example of how biochemists can "design" to increase therapeutic activity and minimize undesirable side actions. Below, for example, we see the important changes that were made in reference to the hydrocortisone molecule to produce fluocinolone acetonide, one of the most active of all topical corticosteroids. As a result, a 0.01% preparation of Synalar (fluocinolone acetonide) has been reported to do the work of a 1% hydrocortisone product containing 100 times more corticosteroid. And it can often do it more effectively.



Hydrocortisone

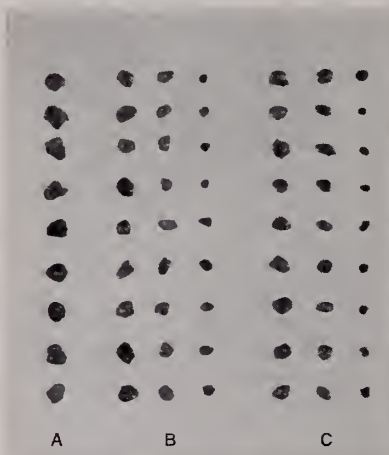


Fluocinolone Acetonide (Synalar)

- a double bond between carbons 1 and 2
- fluorine substitutions at both the 6- α , and the 9- α positions
- the addition of the acetonide at the 16- α , 17- α positions, thus providing one of the most potent topical corticosteroids available.

How bioassay tests are used to "predict" therapeutic potential

Biologic assays are another tool used by researchers to help establish the relative activity of corticosteroids. To date no single method of assaying corticosteroid activity has emerged as the ideal "yardstick" for predicting therapeutic potential. Taken together, however, these methods have proved useful. When such tests are run on various corticosteroids, a definite order of corticosteroid activity becomes evident. Compounds with the highest order of activity may be expected to merit clinical trial to establish their high therapeutic potential. When assayed by these methods, fluocinolone acetonide (Synalar) emerges as one of the most active topical corticosteroids, milligram for milligram, available for clinical application today.



THE THYMUS INVOLUTION ASSAY¹⁻⁴ is run on adrenalectomized rats. The sizes of the glands are measured, and the degree of involution caused by the steroid is determined as an indication of its potency. In the above photo, the comparative involution of thymus glands achieved with hydrocortisone and Synalar (fluocinolone acetonide) is shown. Untreated controls (A) show normal size. Group B— injected with 1, 2 and 4 mg. of hydrocortisone— show progressively smaller thymuses as does Group C— injected with fluocinolone acetonide— but with only 1/500th the dose of hydrocortisone.



THE ANTIGRANULOMA ASSAY¹⁻⁴ also utilizes adrenalectomized rats. Granulomas are induced by subcutaneous implantation of cotton pellets on either side of the thorax. The degree of granuloma inhibition achieved by a steroid reflects its potency. The above photo shows the inhibition of granuloma formation achieved with hydrocortisone and Synalar (fluocinolone acetonide). Untreated controls (A) show large, red granulomas adhering to the pellets. Group B, receiving hydrocortisone and Group C, receiving fluocinolone acetonide, show little, if any, granuloma formation. Fluocinolone acetonide produced the same effect as hydrocortisone with only 1/500th the dose. This assay, as well as the thymus involution assay, measures systemic rather than topical corticosteroid activity. Nevertheless, results by these methods correlate well with other assays and with the milligram potencies of topical steroids in current clinical use.

Worldwide clinical experience confirms the predictable therapeutic potential of Synalar

It is particularly gratifying that the promise of the advanced chemical design and high order of bioassay activity of Synalar (fluocinolone acetonide) has been confirmed by widespread therapeutic application. Indeed, the impressive clinical response rate of Synalar has been documented in no fewer than 232 papers from 22 countries.

PRESCRIBING INFORMATION

For initiation of therapy: Cream 0.025%, 5 and 15 Gm. tubes, 425 Gm. jars; *for emollient effect:* Ointment 0.025%, 15 Gm. tubes; *for maintenance therapy:* Cream 0.01%, 15 and 45 Gm. tubes, 120 Gm. jars; *for intertriginous or hairy sites:* Solution 0.01%, 20 cc. and 60 cc. plastic squeeze bottles; *for infected inflammatory dermatoses:* Neo-Synalar® Cream (0.025% fluocinolone acetonide, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes.

CONTRAINDICATIONS: Tuberculous, fungal, and most viral lesions of the skin, (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. **PRECAUTIONS:** Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for pro-

Representative Clinical Results with Synalar*

Efficacy Documented in over 4,000 Patients

Condition	Number of Publications	Number of Patients	Significant Improvement†
Contact Dermatitis	27	750	713
Eczematous Dermatitis	21	472	409
Seborrheic Dermatitis	18	442	426
Atopic Dermatitis	24	460	426
Psoriasis	36	1,699	1,510
Neurodermatitis	18	351	324
Total	144	4,174	3,808

*Complete bibliography on request.

†Expressed by the authors as excellent, very good, good, complete remission of inflammation, etc.

longed periods of time. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. When severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. **SIDE EFFECTS:** Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. The neomycin in Neo-Synalar Cream rarely produces allergic reactions.

REFERENCES: 1. Lerner, L. J., Bianchi, A., Turkheimer, A. R., Singer, F. M., and Borman, A.: Anti-inflammatory steroids: potency, duration and modification of activities. *Ann NY Acad Sci* 116:1071 (Aug. 27) 1964. 2. Idem: Comparison of anti-granuloma, thymolytic and glucocorticoid activities of anti-inflammatory steroids. *Proc Soc Exp Biol Med* 116:385 (June) 1964. 3. Ringler, A.: Activities of adrenocorticosteroids in experimental animals and man, in Dorfman, R. I.: *Methods of hormone research*, New York, Academic Press, 1964. vol. III. pp. 234-280. 4. Gubersky, V. R.: To be published.

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Results often comparable to
those of systemic corticosteroids
with fewer hazards

Flaps and Grafts

In Head and Neck Surgery

GEORGE A. SISSON, M.D.*
Syracuse, New York

A SURGEON WELL trained in treating a specific area should be equally capable of restoring the regional physiology of his patient and, therefore, be completely able to assume responsibility not only for his patient's surgical health but also for his final appearance.

As head and neck surgery, often extensive and radical, continues to attract an increasing number of otolaryngologists, so does the need for greater knowledge and appreciation of the various successful reconstruction techniques become increasingly essential.

The following outline represents a somewhat simplified classification of the more useful grafts and flaps used by otolaryngologists, with examples of their application in the rehabilitation and reconstruction of the head and neck areas:

Free Grafts

Full-Thickness Graft

Full-thickness grafts are usually selected when small to moderate lesions on the dorsum of the nose, cheek or forehead are excised.

Split-Thickness Graft

Split-thickness grafts are used to cover large defects on the face, neck, scalp, intra-oral region and most donor sites when the pedicle grafts are large. They are used also to line pedicles and as temporary donor dressings in areas where large pedicles have been borrowed. In special instances split-thickness grafts are of value when placed over the dura which is easily and often exposed during radical maxillectomies with orbital exenterations and during radical temporal bone resections.

Dermal Grafts

Dermal grafts, the "added protection" grafts, are most valuable when used as cov-

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Fig. 1-A — Composite graft for through-and-through repair of alar. (Skin, cartilage and mucosa)

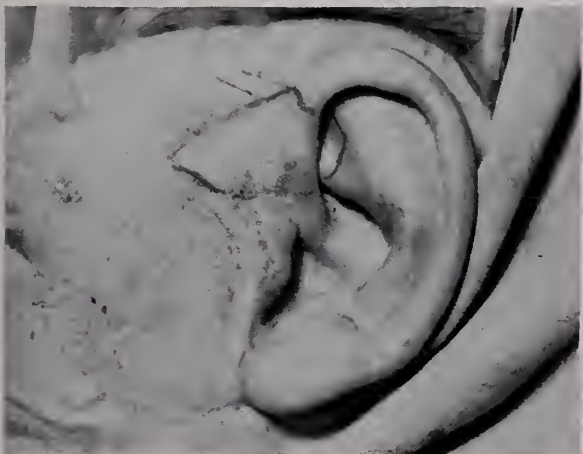


Fig. 1-B — Donor site. (From anterior superior auricle)



Fig. 2 — Small pedicle flap from naso-alar fold to cover lateral dorsum of nose.

erings over the carotid complex and the pharyngeal suture line in cases where preoperative radiation has been given.

Composite Grafts

Composite grafts usually taken from ear auricles, provide an effective three-layer covering for defects in the lower lateral nose cartilages (Figures 1-A and 1-B).

Fat Grafts

Fat grafts from the abdomen are used for obliterating frontal sinuses and for the restoration of facial contours.

Bone Grafts

Bone grafts from a rib or iliac crest can improve nose contours and zygomas as well as fill antrums to raise orbital floors when correcting late deformities from orbit blow-out fractures.

Muscle Grafts

Temporalis muscle grafts have long been used successfully to obliterate the mastoid cavity. These are often rotated on pedicles, although they can be and often are put in as free implants.

Fascia Grafts

Fascia grafts are currently used very successfully to repair the drum membrane in reconstructive surgery of the middle ear. Temporalis fasciae are convenient donor sites.

Pedicles

Small Pedicle Grafts

Small pedicles are used most frequently and most successfully.

A full-thickness flap is rotated to close most defects over the cheek, lid, forehead, naso-alar fold (Figure 2), dorsum of the nose, and most defects after the excision of large lip lesions.

A useful variation, "the island flap" (Figures 3-A and 3-B), is rotated from the center of the forehead with the pedicle buried in a tunnel and the flap applied to the dorsum of the nose.

Flap Grafts

Large regional flaps represent one of the

strongest grafts available for resurfacing large areas about the head and neck that are "in trouble" (Figure 4). This "troubled area" could be the result of heavy preoperative radiotherapy, a postoperative infection creating massive salivary fistulae which often are associated with impending carotid hemorrhages; or it could be a large facial defect after an extensive excisional resection to control a bulky primary or recurrent cancer. This type of problem can be corrected only if there is an immediate transfer of large viable tissue to the "troubled area." The most frequently used regional flaps and examples of their application are outlined below. All of these flaps are stronger if delayed once; but more often than not, it is unnecessary to delay, and satisfactory results are obtained from the immediate transfers.

Large chest pedicles, sometimes referred to as "nipple flaps," are used when an immediate transfer to the neck of 200 to 250 square centimeters of virgin tissue is necessary. Because of its length this flap is capable of resurfacing one complete side of the neck with ease and can be rotated so as to resurface a completely exposed carotid. In addition, it can be extended into the floor of the mouth for anastomosis with the portion of the tongue still remaining: usually an effective procedure when the construction of a preliminary pharyngostoma is attempted (Figures 5-A and 5-B). This chest flap may be based laterally from the anterior shoulder on a 10 to 12-centimeter pedicle with its two inferior limbs extending obliquely parallel for 20 to 22 centimeters, so that the nipple on the ipsilateral side is included in the flap. It is prudent upon raising the flap to remove a 2x3-cm. triangular wedge on the medial aspect since this is the weakest area of the flap. After edges of the donor area are undermined, the final defect is closed with a split-thickness graft from the thigh. The transposed nipple in the neck can be removed at a later date under local anesthesia. Although it is possible to raise chest flaps from both sides at the same time, this is rarely necessary. Usually an associated, smaller cervical flap will suffice to complete most



Fig. 3-A — Island flap with vascular pedicle buried in tunnel and full thickness pedicle graft sutured to dorsum of nose.



Fig. 3-B — Midline incision closed by undermining and suturing. (Two weeks post-operative)



Fig. 4 — "Troubled area." Post-surgery and radiation with impending carotid blow out. Resurfaced by large pedicle flap from chest. (Nipple flap)

resurfacing. Care must be taken when raising the large chest flap to preserve the deep blood supply under the superficial pectoralis fascia; the skin and the subcutaneous tissue are taken down to the fascia. The axillary artery with its branches, the thoracoacromio artery and the lateral thoracic artery, together with the deltoid artery provide this type of pedicle with a generous circulation.

A modification of this flap is a smaller medially-based chest pedicle which is transposed superiorly and is useful when resur-

facing the lower central and lateral neck. This pedicle derives its blood supply from the perforating branches of the internal mammary artery and may also be raised without delay as two separate grafts, one from each side of the upper chest; and they may be formed at the same time.

Large cervical flaps, raised from either side of the neck and transposed to midline or lateral defects, are a convenient and effective means of bringing new tissue to large distressed areas. However, if a patient has



Fig. 5-A — Large lateral chest flap (400 sq. cm.) transferred at time of surgery to resurface heavily radiated tissue. Extends to floor of mouth.



Fig. 5-B — Sutured in place to form floor of mouth.

had heavy neck radiation a surgeon cannot always use this type of rotation. Viability becomes apparent once the flap is raised. Often several centimeters of the distal end must be sacrificed to insure good healing; but if there is doubt it would be prudent to abandon this effort and transfer non-radiated tissue from the chest as has been described.

Cervical flaps may be used as a combined

flap by delaying and lining the distal third with a split-thickness graft or by folding the end of the flap over on itself and transferring to the defect at a later date. Combined cervical flaps are most useful when reconstructing large oral-cheek fistulae, closing pharyngeal fistulae and reconstructing defects in the floor of the mouth.

Recently cervical flaps have been used to reconstruct palates after radical maxillary



Fig. 6-A — Immediate repair of palate after radical maxillectomy and exenteration of orbit by long cervical flap.

Planning: cross-hatched area will rotate medially, proximally tubed, skin side in, as it passes under the mandible.



Fig. 6-B — Cervical flap raised.

resections and exenterations of the orbit (Figures 6-A, 6-B, 6-C, 6-D). When this technique is employed, the flap is rotated into the mouth proximally, tubed skin side in, where it passes under the mandible. This procedure or variations of it are used when primary reconstruction of the floor of the mouth either laterally or medially is necessary. When the base of the flap is posterior, it is called the "nape of the neck" flap; and since mutilation of the breast is unnecessary it is particularly useful in females. Since the post-auricular and occipital arteries provide

the vascular strength of this flap, these arteries must not be injured as the flap is raised from a subnuchal pedicle which extends down to the fascia over the trapezius.

Large scalp flaps are frequently used to reconstruct an entire nose as well as other large deficit areas on the face. Smaller defects are resurfaced by utilizing median or laterally based forehead flaps (Figure 7). Care must be taken not to injure the superficial temporal artery since the scalp flaps' luxurious blood supply depends upon it regardless of the adaption selected for use in

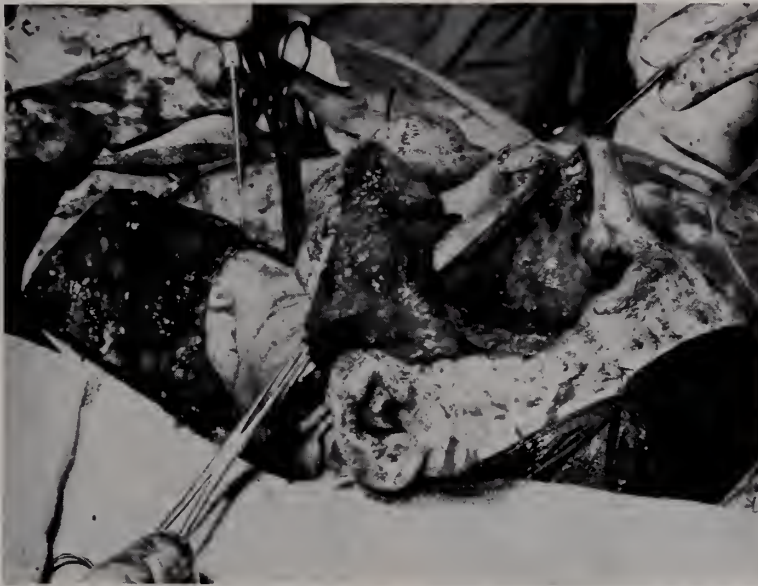


Fig. 6-C — Cervical flap passed under mandible.



Fig. 6-D — Completed suturing of flap.

this procedure. The classical "sickle flap" or one of its modifications (Figures 8-A and 8-B) is used most often in these situations.

Any one of these large scalp flaps may be combined with a split-thickness graft when a through-and-through defect is to be reconstructed. In a combined technique the transfer usually is staged or delayed until the under surface of the flap, whether covered by a split graft or a folded end, has healed.

Tubular Grafts

Tube grafts may be single or bi-pedicle and merit reference because of their high reliability when used in difficult recipient areas. This graft, once the "work horse" of reconstruction techniques, is not as popular today because a patient must undergo multiple transfer stages, the final reshaping of the migrated tissue into a desirable result is difficult to achieve and the techniques employing the large regional pedicle grafts are better understood today and preferred.

The single pedicle tube may be fashioned from either the upper anterior chest or the

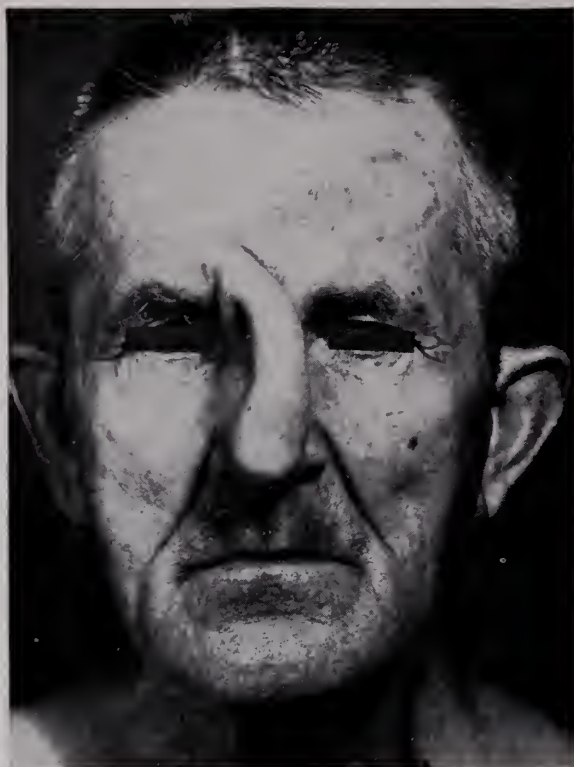


Fig. 7 — A laterally based forehead flap for resurfacing of 4/5 of upper nose.



Fig. 8-A — Raising a modified sickle flap (note temporalis muscle preservation on donor side).



Fig. 8-B — Donor area covered temporarily with Thiersch graft.

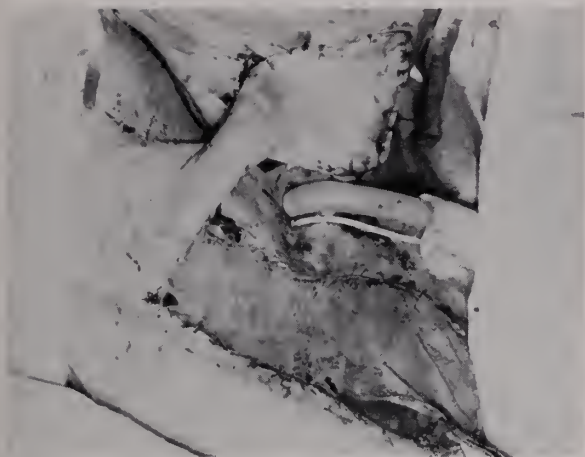


Fig. 9 — Single pedicle tube — transferred as paddle flap.



Fig. 10-A — Completed bi-pedicle acromiothoracic tube.



Fig. 10-B — First transfer.

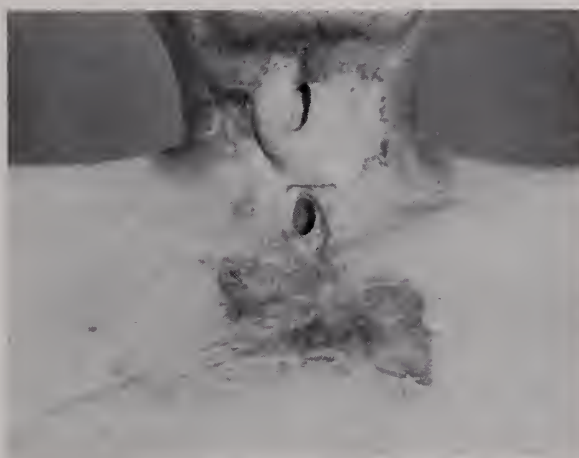


Fig. 10-C — Second transfer healed, ready for final midline suturing.



Fig. 11-A — Bi-pedicle cervical-acromio tube.



Fig. 11-B — Large donor defect closed using rotated lateral pedicle flap from chest wall.

cervical area. A graft from the cervical area is delayed in the first stage as a short bi-pedicle tube which can conveniently be raised horizontally across the anterior cervical area or the acromioclavicular region if necessary. At the second stage a paddle can be formed and lined for use as a combined graft. This lined paddle (Figure 9) can be rotated into the desired position for reconstruction of a through-and-through defect. Careful planning and patience between stages are necessary if this flap is to be used successfully.

The bi-pedicle tube flap can be raised obliquely across the chest wall as an acromioclavicular (Figures 10-A, 10-B and 10-C) or acromioclavicular tube (Figures 11-A and

11-B). If the patient is obese, careful trimming of fat is necessary when the free edges are tubed, because the contents of the tube should not be subjected to any pressure. If large facial or neck defects are to be reconstructed, two bi-pedicle tubes can be raised at the same time from either side of the chest. If healing is complete after a two-week delay these tubes are transferred in stages to the "troubled area." Multiple stages are usually necessary before the final result is completed. This graft, however, is very strong so that even if a portion of it does not survive in a poor recipient area the remaining tissue is usually sufficient for the reconstruction.

"Our general construction is determined by the fact that we are made of living matter, must accordingly be constantly passing a stream of fresh matter and energy through ourselves if we are to live, and must as constantly be guarding ourselves against danger if we are not to die. About 5 per cent of ourselves consists of a tube with attached chemical factories, for taking in raw materials in the shape of food, and converting it into the form in which it can be absorbed into our real interior. About 2 per cent consists in arrangements — windpipe and lungs — for getting oxygen into our system in order to burn the food materials and liberate energy. About 10 per cent consists of an arrangement for distributing materials all over the body — the blood and lymph, the tubes which hold them and the pump which drives them. Much less than 5 per cent is devoted to dealing with waste materials produced when living substance breaks down in the process of producing energy to keep our machinery going — the kidneys and bladder and, in part, the lungs and skin. Over 40 per cent is machinery for moving us about — our muscles; and nearly 20 per cent is needed to support us and to give the mechanical leverage for our movements — our skeleton and sinews. A relatively tiny fraction is set apart for giving us information about the outer world — our sense organs. And there is about 3 per cent to deal with the difficult business of adjusting our behaviour to what is happening around us. This is the task of the ductless glands, the nerves, the spinal cord and the brain; our conscious feeling and thinking is done by a small part of the brain. Less than 1 per cent of our bodies is set aside for producing the race. The remainder of our body is concerned with special functions like protection, carried out by the skin (which is about 7 per cent of our bulk) and some of the white blood corpuscles; or temperature regulations, carried out by the sweat glands. And nearly 10 per cent of a normal man consists of reserve food stores in the shape of fat."*

*Julian Huxley in *Variations on a Theme by Darwin* — in *A Treasury of Science* by Harlow Shapley, Harper and Brothers, N. Y. p. 561.

Mid Facial Fractures

JEROME A. HILGER, M.D.*
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VISUAL, MANUAL and x-ray examination will determine the best program for mid-facial skeletal repair. The objectives are good nasal function, good dental occlusion, normal ocular fusion, and the best cosmetic result obtainable.

The Nose

The composite of bones and cartilage collectively termed "the nose" leads all skeletal parts in fracture frequency. The superior one third to one half of the projecting portion of the nose is formed by the frontal processes of the maxillae surmounted by the nasal bones, which unite atop the middle ethmoidal plate of the bony septum. This complex may shatter in the manner of an eggshell as a result of central facial third impact (Figure 1). The characteristic front-seat passenger smash into the dashboard produces this injury. The frontal process of the maxilla, if sufficiently sturdy may fracture at the infra-orbital abutment with the malar bone and impact with the lacrimal bone into the ethmoid labyrinth.

The usual athletic injury fracture dislocates the nasal bones from on top the frontal processes of the maxillae; the latter may fracture from the main body of the maxillae as well. In either case, the septal plate of the ethmoid is carried in the direction of displacement. This must be reckoned with in the course of reduction.

Upper Nasal Segment

Injuries of the upper nasal segment are easy to diagnose and delineate by palpation and inspection. X-ray examination is much less informative though perhaps more impressive. Doubt whether fracture has occurred can be resolved by looking and feeling again in a few days when soft tissue swelling has subsided. This delay does not prejudice the final result.

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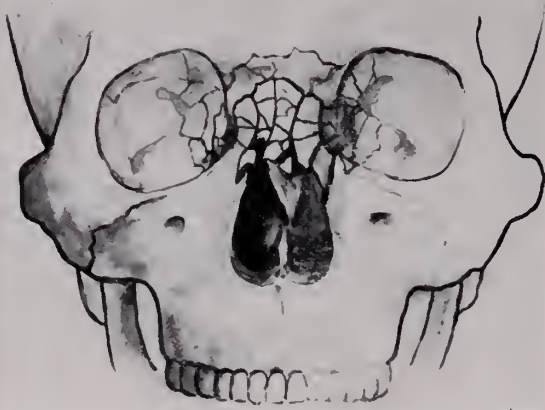


Fig. 1 — Comminuted (eggshell) nasoethmoidal fracture.

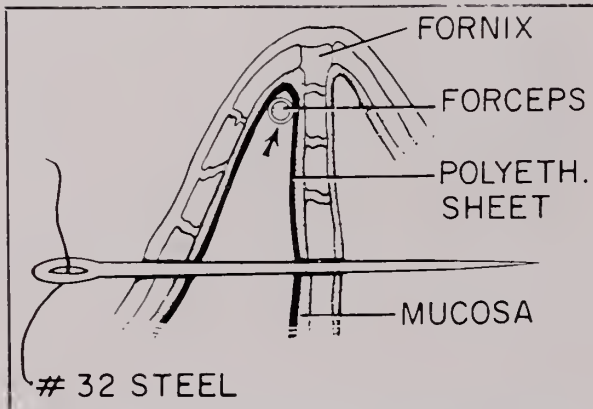


Fig. 2 — Method of elevation of comminuted naso-maxillary elements and insertion of wire transfixion at the base.



Fig. 3 — Completion of wire transfixion technique for comminuted nasoethmoidal fracture.

Realignment of these fractures can be accomplished by intranasal and external manipulation and molding. General anesthesia is frequently desirable. Usually the fragments maintain reposition without splinting. An external molded dressing is sometimes useful to minimize dorsal edema, which can result in slippage of fragments. In addition, it can produce undesirable thickening due to organization of transudate. A modest intranasal support by a petrolatum gauze strip high in the fornix can be useful to prevent impacted fragments from falling back into the chamber. However, intranasal packing stuffed into the nasal space to counter bleeding is a useless and harmful routine measure.

If comminution is extensive (Figure 1) and manual elevation of fragments will not maintain position with these simple efforts, direct wiring and pinning are necessary. Two 32-gauge steel wires threaded on straight needles are passed through the base of the bony nasal mass (Figure 2). Comminution makes this maneuver easy, or the needle can be drilled through. The wires are threaded through molded lead plates, which are snugged to the nasal skeleton to support an agreeable contour (Figure 3). Incorporation of a sheet of synthetic film draped over the intranasal elevators used to advance the mass as the drill wires are placed at the base will keep the torn mucosal surfaces of the vault separated during healing and prevent adhesive obliteration of the anterior respiratory vault.

Lower Nasal Segment

The lower half of the external nose is frequently injured without upper half fracture. The magnitude of this injury is often overlooked, as most of the distortion is intranasal. Externally there may be no obvious displacement — only swelling and tenderness. A palpating finger must always be run down the nasal dorsum (Figure 4). A soft point immediately caudal to the end of the nasal bones means that cartilaginous septal fracture and dislocation have occurred (Figure 5). Intranasal septal swelling will fill the nasal vestibules, due to a ballooning hematoma between the septal flaps (Figures

6-a and 6-b). Therefore, an early intranasal open reduction of this injury is mandatory (Figure 6-d). Lack of diagnosis and neglect result in external nasal deformity and septal airway obstruction (Figure 6-c). Rhinoplastic surgery for the deformity of neglected upper nasal injury is uniformly satisfactory. Rhinoplastic and septoplastic surgery for correction of lower half injury is always a compromise. Once the dorsal ridge hematoma soft spot absorbs and organizes, the inspiratory vault of the nasal vestibule is forever lowered (Figures 6-c and 7). Though the later plastic correction obliterates the saddle of the dorsum and narrows the accorded septum, it cannot restore the height of the intranasal fornix. Diagnostic x-ray is useless in this injury. The keys to diagnosis are the soft spot in the lower half of the nasal ridge into which the palpating finger falls as it slides down the nasal dorsum and the complete obliteration of the nasal airway by the hematoma between the septal flaps.

Nasal Septum

Septal incision, as for a classic submucous

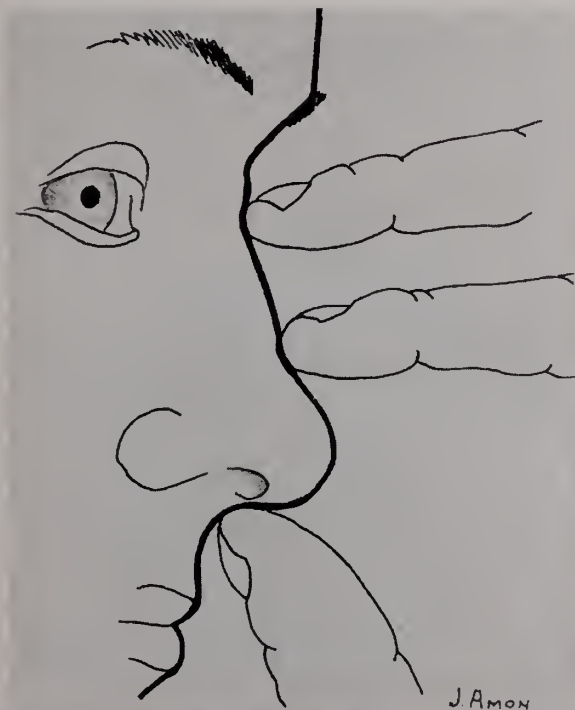


Fig. 4 — Palpation of the cartilaginous nasal dorsum and caudal end of the septum to identify fracture of the cartilaginous nasal segment.

resection, evacuates the subperichondrial hematoma and exposes the multiple fragments of cartilage. Successive replacement of fragments from dorsum to floor is maintained by mattressing chromic sutures through mucosal flaps and cartilage at each fracture line (Figure 6-d). This restores the anatomic relationship of the quadrilateral fragment jigsaw and binds the mucoperi-



Fig. 5 — Dorsal hematoma "soft spot" denoting fracture dislocation of the cartilaginous septum. The mucosa of the intranasal respiratory vault at the upper lateral-septal cartilage juncture is dissected and ballooned downward into the airway.

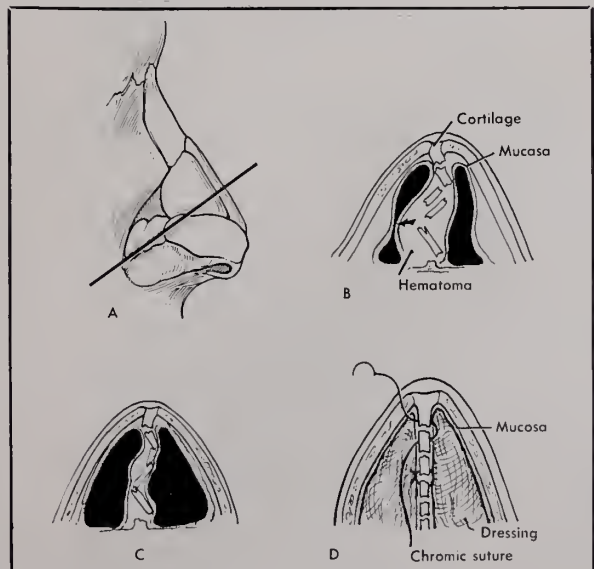


Fig. 6-a, b, c and d — (a & b.) Cross section of comminuted fracture of the nasal septum; (c.) Organization in septal disarray with lowering of the respiratory vault; (d.) Open reduction, hematoma aspiration, and mattress realignment of the cartilaginous septum.



Fig. 7 — The relative nasal "hump" resulting from lowering of the cartilaginous dorsum as a result of dislocation and comminution of the septal cartilage.

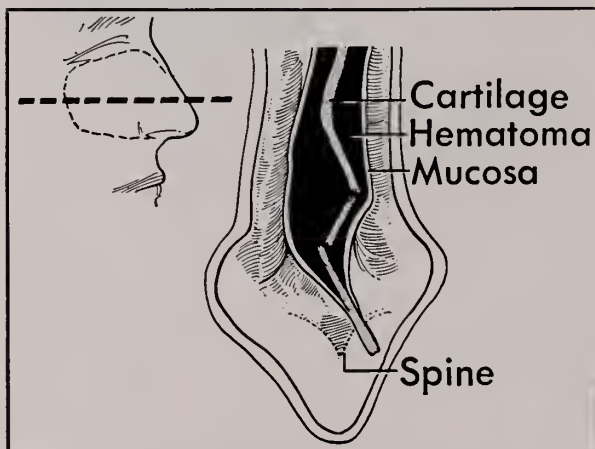


Fig. 8 — Comminuted fracture dislocation of the cartilaginous septum resulting from blow delivered to the caudal end.

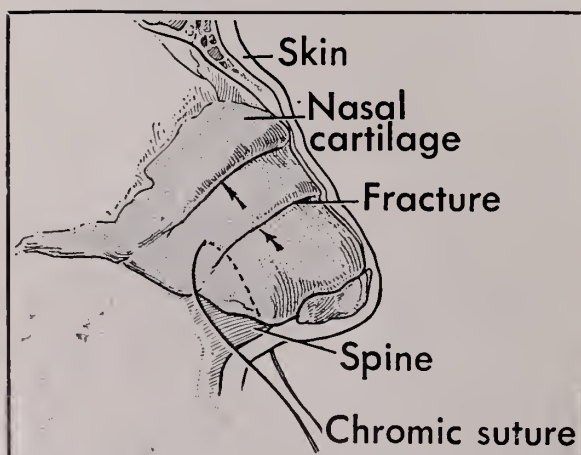


Fig. 9 — Chomic suture transfixion of the cartilaginous septum preparatory to anterior traction — reduction of cartilaginous fracture in Figure 8.

chondrium to the cartilage to preclude post-operative hematoma and position change.

Where the injurious blow has been delivered not at the dorsum but at the caudal end of the nose, lip contusion, sometimes upper incisor tooth and alveolar fracture, and quadrilateral septal cartilaginous and anterior nasal maxillary spine fracture and displacement are not uncommon. The cartilaginous septum is accordioned posteriorward (Figure 8). Palpation of the columellar end shows the absence of firm septal edge (Figure 4). Reduction of the posteriorward accordioning will not maintain without loop suture fixation. This is accomplished by inserting a far posterior septal chomic transfixion suture (Figure 9) which is then brought forward and passed through the vestibular floor skin beneath the spine and into the opposite vestibule, there to be drawn taut to "unpleat" the accordion (Figure 10).

"Central-Third" Fractures of the Face

The pyramid in the center of the middle facial third is comprised of the maxillae, the nasal, lacrimal, and ethmoidal bones. Straight, forceful projection of the face into an unyielding receiver may impact the nasomaxillary mass with or without free fracture of the palatal segment.

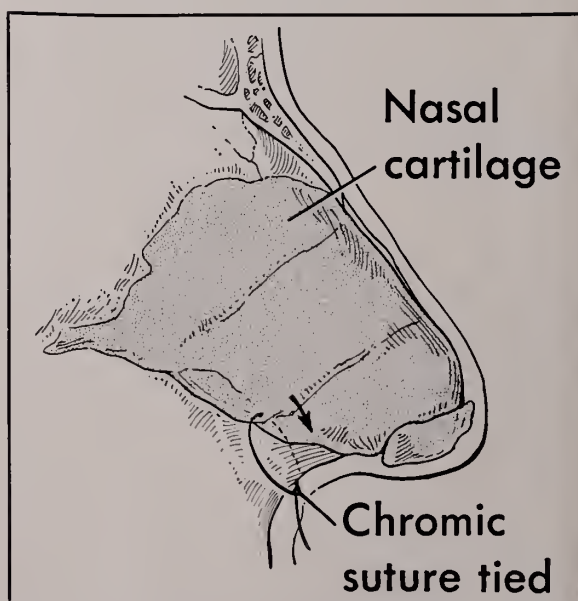


Fig. 10 — Closure of suture passed through the nasal vestibular floor to embrace the anterior nasal spine and "unpleat" the accordion fracture of the quadrilateral cartilage.

Advancement techniques by postpalatal hook, intranasal-intraoral grasping forceps, and intranasal elevator can be supplemented by "molding" pressures deep to the inner canthal areas to reform the crushed ethmoid mass. Free segments of the frontal processes of the maxillae can best be retrieved from the nasal space and repositioned by "bimanual" manipulation with the fifth finger deep in the nasal vault and the fingers of the opposite hand along the orbital rim. Precise replacement can be further assured by infraorbital incision in the lower crease of the orbicularis oculi and direct visualization (Figure 11). This allows wire loop fixation at this point — either single or multiple as necessary to complete the reformation of the infra-orbital rim and its union to the nearest solid lateral abutment (Figure 12).

Glabellar Area

In the glabellar area similar incisional view of the nasal root (Figure 11) and direct wire loop can be valuable in fixing the pyramid to the frontal skull base if gaping requires closure (Figure 12). This can be combined with nasal mass transfixion and molding with lateral malleable metal splints as already suggested, when the bony nasal mass is "egg-shelled" (Figure 3).

It is important to disimpact the recessed nasomaxillary mass at the first opportunity. Early fusion occurs. A bulging of the ethmoidal labyrinth and retrocession of this



Fig. 12 — The maintenance of anatomic realignment with permanent wire loop fixation.

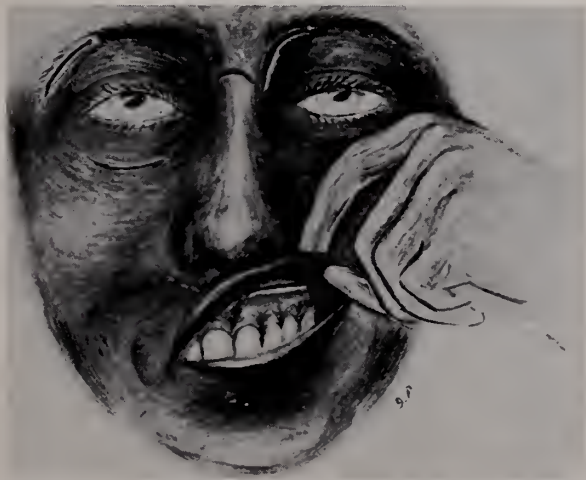


Fig. 11 — Incisional access lines providing direct exposure for anatomic reduction and wire loop fixation.

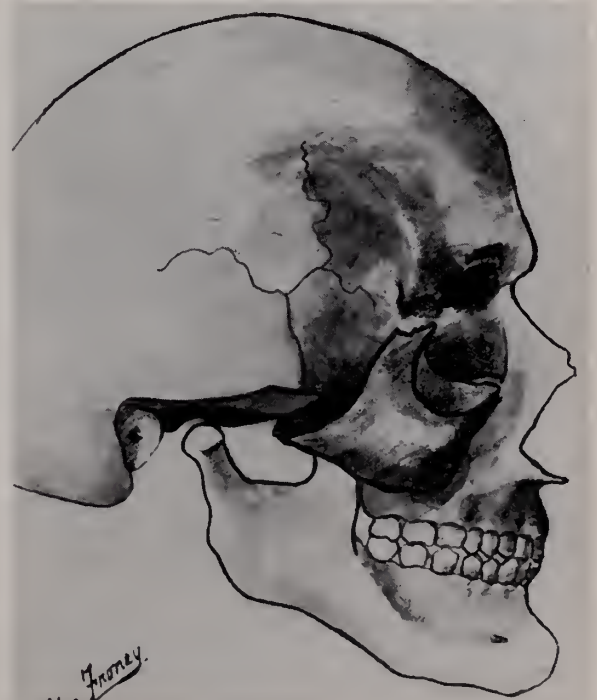


Fig. 13 — The fracture zones of the abutting malar-maxillary complex.

central mass are impossible to correct by later plastic repair. Bony union occurs in a matter of weeks due to the thin plates, extensive periosteal surfaces and rich blood supply.

Cribriform Plate

When this type of fracture includes fracture of the cribriform plate and cerebrospinal fluid leak, early reposition is particularly imperative. The breach in the floor of the anterior cranial fossa will more readily and surely heal and seal if anatomic reposition has been accomplished. If stereoscopic skull films demonstrate a bone fragment displacement and intrusion into the anterior fossa, the facial realignment should be performed in conjunction with intracranial removal of the intruding bone from the floor of the anterior cranial fossa. This latter procedure is accomplished neurosurgically by hairline incision and lowering of the total forehead flap.

Pyramidal Area

Whatever the upper aspect of the pyramidal fracture demands for repositioning and fixation at the intermaxillary level, the teeth must be fixed in occlusion. Arch-bar

application provides a good means. If there is no concurrent mandibular fracture, the versatility of the arch bars allows intermittent use of the intermaxillary elastic binders during the late healing period.

Fractured edentulous maxillae present no occlusion problem whether the mandible does or does not have teeth. Intermaxillary fixation is not necessary. Anatomic reduction and direct fixation can be followed by denture revision after healing.

The Malar Bones

Laterally the malar bones form the buttress and contour of the cheeks. The human has a marvelously rapid protective reflex that turns the head at the instant of impact. The brunt of many blows is borne by the malar bones. Their attachment points — frontal, temporal, and maxillary (infra-orbital and alveolar) — are weaker than the body of the bones (Figure 13). Only occasionally is the bone fragmented. Displacement, however, can be extreme because the large underlying maxillary sinus space provides no support. Rapid swelling tends to obscure the true extent of the cave-in. The line of fracture in the orbital floor tears the

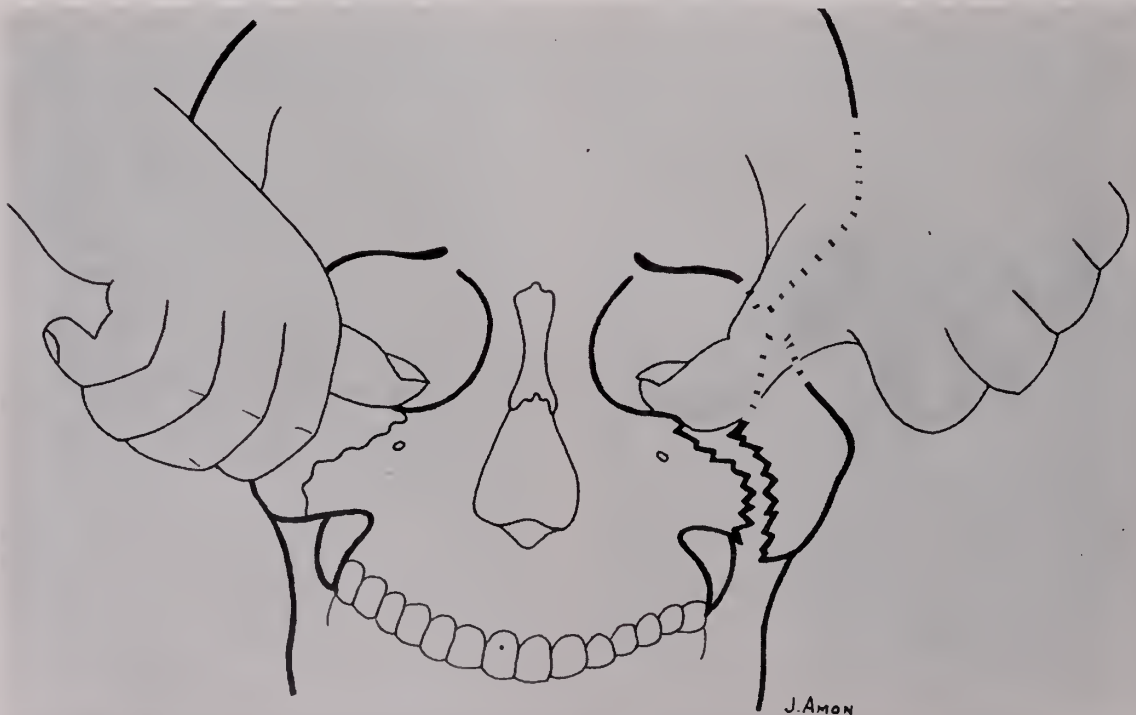


Fig. 14 — Method of examining the infra-orbital rim for malar fracture with comparative thumb palpation from position behind the patient.

periorbita. Hematoma supports the globe at normal level for a week or two, but when it resorbs the globe drops. This global displacement and the shift of the bony attachment of the inferior oblique muscle can result in diplopia of very disabling character. The same hematoma dissects under the bulbar conjunctiva to the limbus. This subconjunctival hemorrhage should warn the examiner that here at least is one swollen and ecchymotic eye that should not be made the butt of doorknob jokes. The humor incident to a "black eye" loses much of its flavor when the patient returns in two weeks with a flattened face and diplopia.

A chin-nose position film as of the maxillary sinuses is quite diagnostic of malar fracture. The presence or absence of displacement should not be determined finally by the film, however. Its angle may not define significant malposition. The palpating thumb placed along the infra-orbital edge may reveal a step-down that is not well shown on the film (Figure 14).

Infra-orbital Rim

Since the weak point of fracture on the infra-orbital rim is at the infra-orbital foramen, hypesthesia of this sensory nerve is usual with malar fracture. Hence numbness of the upper lip and nasal ala on the side of



Fig. 15 — Techniques of malar fracture realignment. Reversal of the injury force is the basic objective.

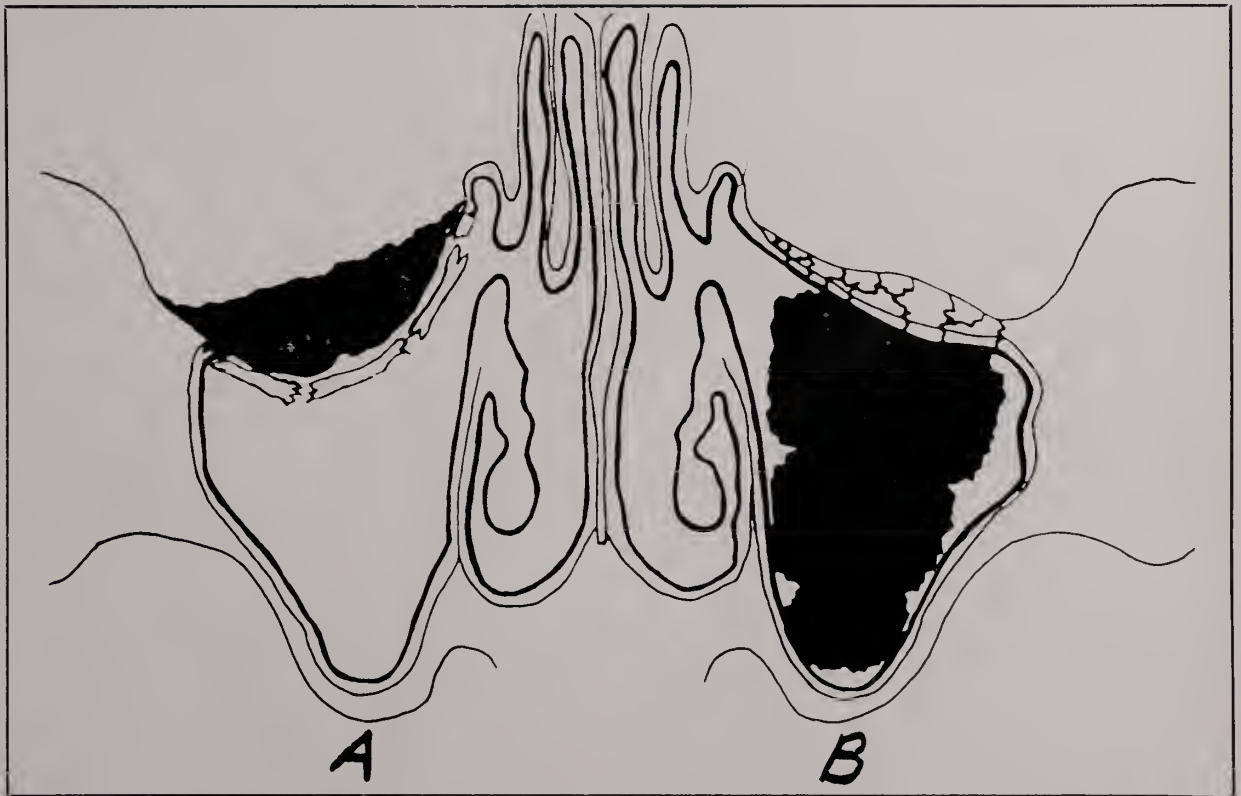


Fig. 16 A and B — (A) Orbital floor implant with silicone rubber sponge for long-standing orbital floor depressions. (B) Intramaxillary antral support of recent orbital floor ("blow-out") fracture with indwelling silicone rubber palisade in three insertional layers.

the injury is an important diagnostic sign. So also is the presence of blood in the maxillary sinus due to tear of the mucoperiosteum. Sufficient depression of the malar arch can impinge on the mandibular coronoid, and mouth closure will then be difficult.

Reposition of the malar bone can be accomplished in several ways; there is no best way for all fractures. The objective of reversing the injury force to realign the fragments demands familiarity with a number of approaches (Figure 15). A lateral blow can be reversed through a temporal hairline and temporal fascia incision with the elevator placed beneath the malar arch. Inferior displacement of the body can sometimes be corrected by manipulation with a bone hook externally or elevation in the buccal sulcus intra-orally. Posterior impaction of a substantial fragment of the infra-orbital rim may require direct exposure through a well-placed infra-orbital incision and retrieving of the fragment with a short strong hook. This exposure allows direct wiring across the frac-

ture line. As with nasomaxillary fragmentation this is accomplished with a drill, fine drill points, and fine steel wire loops (Figure 12).

It is inadvisable to attempt manipulation of the malar bone with a towel clip. This endangers facial nerve filaments when the tenaculum slips. Entering the maxillary sinus through the canine fossa is necessary only in special instances. The maxillary opening requires sacrifice of bone in opening the sinus that would be advantageous for support of the repositioned malar.

If the comminuted shell of the orbital floor is lost into the maxillary antrum ("blow-out fracture") it is better to use incisional access to elevate the orbital contents and visualize the fragmentation directly. Canine fossa opening for digital manipulation and elevation of the fractured segments may be helpful. The inferior oblique muscle and attachment must be anatomically replaced. Three-segment palisade intra-antral support with fine, closed-mesh silicone rubber sponge left

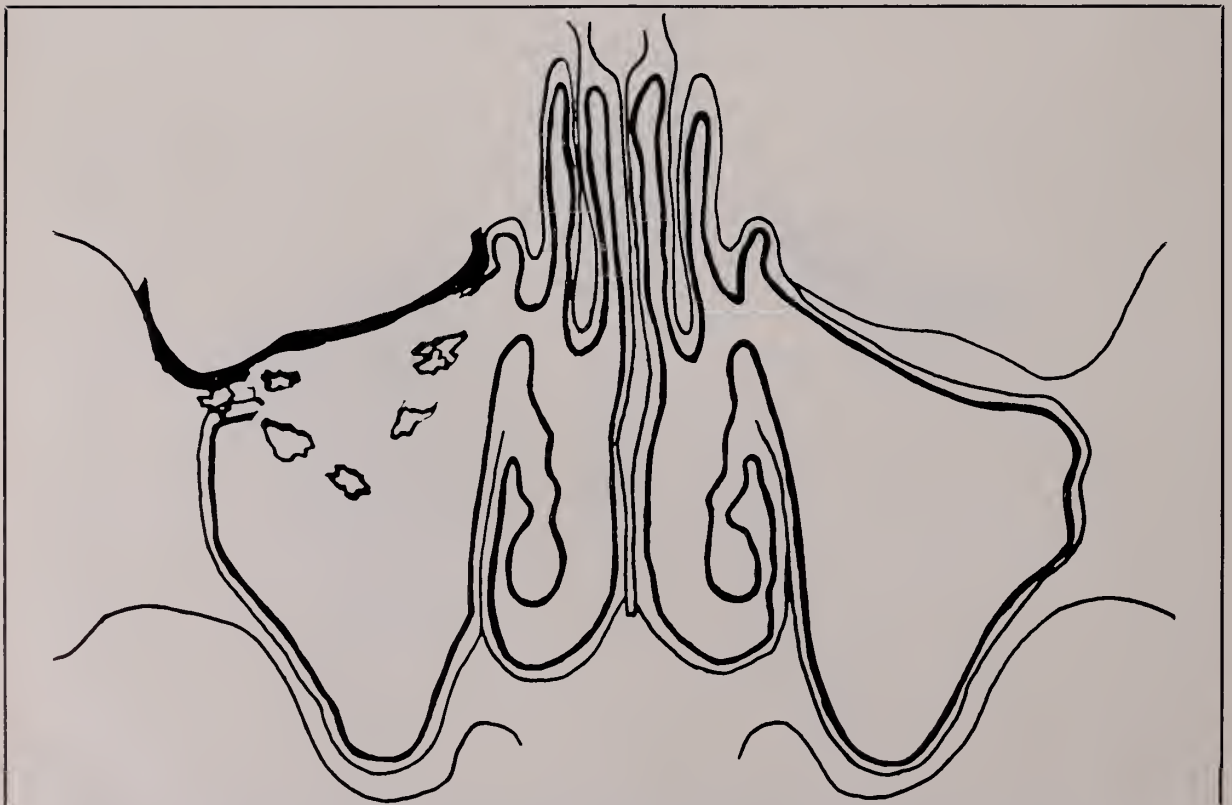


Fig. 17 — Silicone rubber sheet substitution for loss of orbital floor fracture fragments in acute injury.

in place six to 10 weeks will eventuate in a good result (Figure 16-b). If support fragments are deficient the orbital floor can be supplemented with a properly placed silicone rubber sheet (Figure 17). When necessary the fragments of the infra-orbital rim are wired directly into position (Figure 12).

Frontomalar Fracture

Occasionally the frontomalar fracture line will not hold in anatomic reposition after reduction. Direct wiring to the frontal abutment through a lateral brow incision (Figure 11) with or without infra-orbital wiring (Figure 12) is then useful. On rare occasions it can be supplemented with binder traction from a screw inserted in the body of the bone to a head cap appliance. An impaling Kirschner wire carried across to firm supportive bone on the opposite side is sometimes a simple and useful fixation method.

Solid healing in malposition due to neglect of the acute malar fracture is best corrected by osteotomy refracture along the four main fracture lines and reclamation of the malar bone itself for replacement and direct fixation (Figure 12). The results are generally superior to those obtained with implantation of iliac bone or diced cartilage.

When the position of the main body of the malar-maxillary complex poses no problem, but long-standing orbital floor deficiency cripples ocular fusion and disables cosmetically, elevation and support can be helpful. This may be effected with autogenous or despeciated bone implant or silastic sponge implant. The latter is shaped and then divided into two segments by anterior-posterior division. One half is inserted through a medial two-third infra-orbital working incision and crowded with its taper laterally. Then the medial half is inserted and the cut edges matched along the division line (Figure 16-a).

Complex Fractures

The challenging injuries of the facial skeleton are those that combine injury to all or most of the component bones (Figure 18).

Multiple fractures of the facial skeletal components or total fracture are not uncommon. Extraordinary disruption is compatible

with life and occasionally occurs in the absence of intracranial or other injury.

Direct inspection, palpation, and x-ray study serve to orient one with the problem and define the repair sequence. The order of treatment is airway establishment, blood replacement, general assessment, adequate restorative pause, and then integration of the reparative procedures in one orderly operative sequence.

Skeletal repair techniques should not be inordinately complex; simplicity in reduction method and in fixation methods should be the rule. A certain amount of gadgetry is necessary. It can be grossly overdone; then the apparatus becomes more of a problem than the injury. A "Rube Goldberg" solution is a poor substitute for simple direct fracture exposure and wire loop or pin fixation. Incisional access (Figure 11) will expose the



Fig. 18 — Complex facial injuries may be unilateral as above or bilateral. The mandible may or may not be involved. The whole problem is divisible into individual component parts — each amenable to relatively simple solution.

usual fracture sites directly. Anatomic realignment with direct vision is more certain than is tactile realignment through an edematous, ecchymotic soft tissue mass. Permanent wire fixation is accomplished through the incisional exposure with fine loops passed through fine drill holes (Figure 12). In multiple fractures the most lateral or superior fragment is attached first to the unfractured skeleton. The other fragments are attached in succession — downward and medialward.

Soft Tissue Repair

When general circumstances make surgical delay advisable, facial soft tissue injury can be protected with a compression dressing for twenty-four hours. If longer delay is unavoidable the soft parts can sometimes be cleaned, trimmed and repaired at bedside with the aid of local anesthesia. Access to the skeletal fragments through the lacerations is frequently important for direct wiring and ideal fixation; on occasion it is necessary to open repaired lacerations for this purpose. The greatest aid to ideal soft tissue approximation is perfect skeletal realignment.

Debridement of facial wounds can be conservative but must be thorough as to depth. All surface tattooing should be removed. Suture materials of 6-0 and 5-0 gauge with comparable needles should not be exceeded. Gentle handling of tissues is mandatory. Magnifying loupes increase the precision of repair (Figures 19-a, 19-b and 19-c).

Closure must be in layers with no tension exerted at the skin surface. For repair

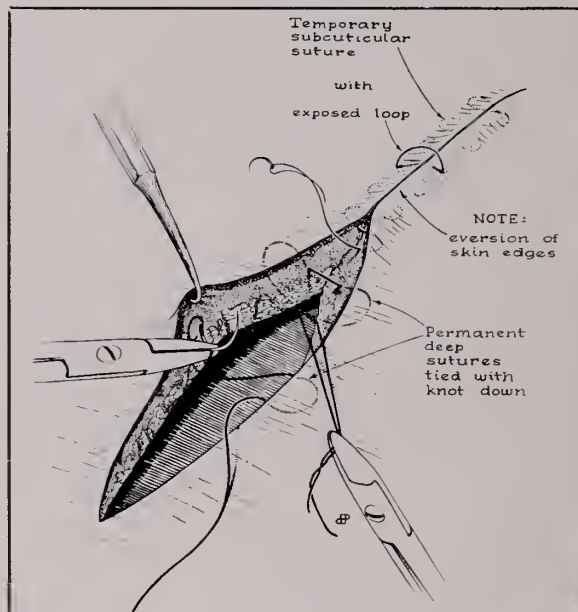


Figure 19 (b)

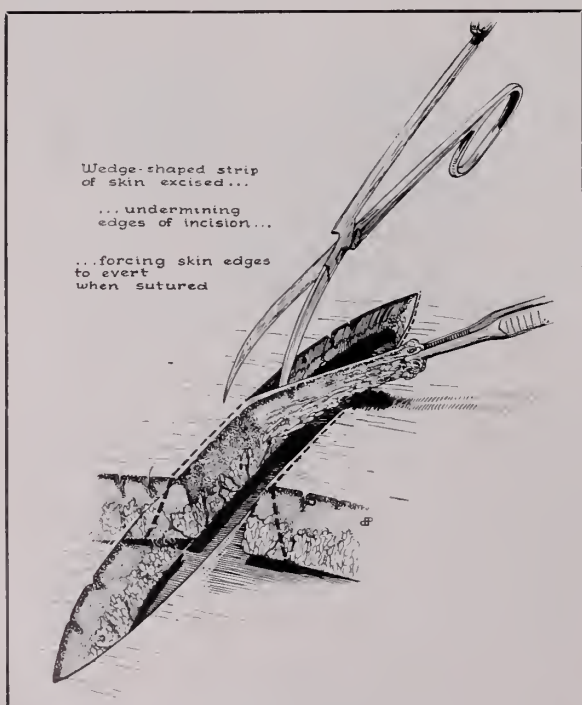


Figure 19 (a)

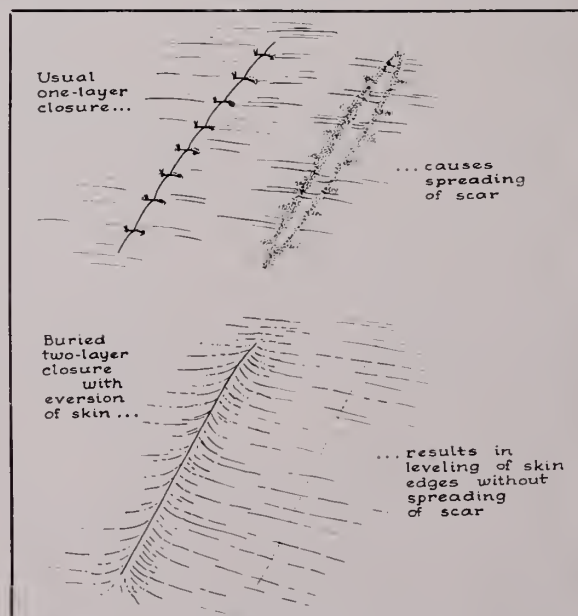


Figure 19 (c)

Fig. 19 (a), (b), (c) — The basic principles of soft tissue repair — careful debridement, closure in layers, fine instrumentation and suture, loupe magnification.

of lacerations into mucosal lined spaces, thorough mucosal approximation is the primary step. Skin sutures should not be placed wide of the laceration margins. Subcuticular techniques are excellent in soft tissue repair. The outer suture can remain for a week. Adhesive supports can be applied in addition to skin sutures. Edema and serum pooling are prevented by elastic dressings; circumferential are best when possible. Crusting at the repair lines is undesirable and is prevented by moistening the dressings at the incision lines with dilute neomycin solution for the first three days. Thereafter, soften-

ing ointment of neomycin — gramicidin — polymixin-type is desirable. Interrupted sutures must be divided in 48 hours and removed in 72 hours. Adhesive bridging is applied for support at the time of suture division. Antibiotics and good facial blood supply reduce infection to a minimum as long as debridement is adequate and mucosal surfaces have been properly approximated.

After the primary three weeks healing is complete, the facial scars should be massaged lightly with bland skin cream for five minutes four times a day to improve mobility and elasticity in the healing scar.

Mr. Barzun Comments Community Life in Medicine

We came alone into this world and expect to leave it the same way. When we are ill, we feel similarly alone in our misery; being sick is a highly individual affair, which makes us long for personal attention, not just "personalized" on the surface; and this is what our system overlooks, what too many doctors fail to understand.

Now no one but an ignorant savage is "down on doctors" or begrudges them their authority. . . . One understands that each good practitioner has probably more patients than he can handle. It is natural, efficient, normal to apply to them the methods of mass production. . . . Medical techniques have the impersonality of science — tests, charts, averages. All this is right and proper, but one must ask how far the doctor's training as a healer is damaged by it. The patient survives, but why should he spend his worst moments in an atmosphere wholly mechanical and metallic?

If he goes to the hospital, he finds it has become a factory run by engineers. . . . Say you have been in pain, unable to sleep. Finally you drop off. Ten minutes pass: you are brusquely waked up: the nurse is there to give you a sponge bath. It is routine. You are bright enough to see that if every patient chose his own time, the system would go to pieces. But the fact remains that you have been deprived of one of the rights of the sick. Hardly back from death's door, you have been forced to "co-operate" again. Your illness is not your own, it's a segment of community life.

Jacques Barzun: *When the Doctor Is a Pill* (in *God's Country and Mine*) 1954

Without my work in natural science I should never have known human beings as they really are. In no other activity can one come so close to direct perception and clear thought, or realize so fully the errors of the senses, the mistakes of the intellect, the weaknesses and greatnesses of human character. — Goethe

The tyrant dies and his rule is over; the martyr dies and his rule begins.

— Kierkegaard



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Contraindicated in presence of renal impairment, peptic ulcer, ulcerative colitis, or mental depression, and in patients with porphyria or those sensitive to any component. **Warning:** Coated potassium tablets, sometimes administered in conjunction with anti-hypertensive therapy, may be associated with small bowel lesions which have led to obstruction hemorrhage, and perforation. Surgery has been required and deaths have occurred. Such tablets should be used only when indicated and when adequate dietary supplementation is not practical. They should be discontinued immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occur. **Precautions:** Exercise caution in hepatic disease, diabetes, surgery, coronary artery disease, epilepsy, E.S.T., and in patients receiving digitalis. **Side Effects:** Electrolyte imbalance, hyponatremia, hypochloremic alkalosis and/or hypokalemia, hyper-

uricemia and gout, bradycardia, drowsiness, skin rashes, hangover, systemic disturbances, weakness, leg cramps, diarrhea, epistaxis, dizziness, urticaria, dry itching skin, nausea, vomiting, palpitation, superficial skin bruises, headache, dehydration, paresthesias, photosensitivity, pancreatitis, jaundice, xanthopsia, thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, nasal congestion, hypotension, lassitude, loose stools, anorexia, bizarre dreams, peptic ulcer, ulcerative colitis, mental depression. (Ammonium chloride, which may be administered to reverse hypochloremic alkalosis, should not be given to patients with hepatic disease.) **Before prescribing or administering, see package insert.** †Warning: May be habit forming. **Usual Adult Dosage:** Butiserpazide®-25 or Butiserpazide®-50: 1 tablet daily or b.i.d. **References:** 1. Johnson, H. J., Jr.: Penna. M. J.: 67:35, 1964. 2. Coodley, E. L.: Curr. Ther. Res. 4:460, 1962.

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Management of Alveolar Fractures

ALBERT HOHMANN, M.D., D.D.S.*
St. Paul, Minnesota

INJURIES TO THE inferior and superior maxilla are seen more frequently now in association with the increasing number of traffic accidents. There is a higher incidence of limited injuries to the jaws because more motorists are wearing seat belts. Often they suffer alveolar ridge or nasal fractures. This increase of limited trauma to the facial bones should alert the family physician to the fact that he, rather than the specialist in the large emergency centers, will often be called to render initial treatment and advice. Frequently, cases which at first glance appear as simple problems turn out to be complicated.

Physicians attending accident victims are well trained in establishing an adequate airway and caring for soft tissue and bone injuries. The dental aspects, however, may escape attention and therefore be neglected.

Hazards of Alveolus Fracture

1. Fractures of the alveolus of the inferior and superior maxilla are the most common jaw injuries in children and young adults.
2. One or several teeth may be damaged or displaced.
3. In children under twelve years of age, both the first and second dentition can be injured.
4. Teeth, especially those of the second dentition, represent one of the most precious units of the human body and must be preserved if possible.

Diagnosis of Alveolar Fractures

Inspection and Palpation of the Alveolar Ridge

Extra and intra-oral examination is tedious and sometimes painful. Because of the pain, swelling and trismus, especially if

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fractures are present, local or general anesthesia may be necessary for an adequate examination. An abnormally mobile alveolar segment indicates fracture. Most commonly the alveolar segment may be: (a) totally avulsed, (b) pedicled on one mucoperiosteal flap, or (c) suffering only vertical or horizontal linear fracture.

Determination of Dental Injury

Dental injuries can involve: the enamel, the dentin, and the pulp of one or several teeth. The degree of damage to these three structures can range from a hair-line crack in the enamel and dentin of the crown to complete fractures involving the crown, the root, or both. The use of a bright headlight, together with head and laryngeal mirror, for transillumination of the teeth is very helpful.

Assessment of the Degree of Malocclusion

In order to detect any malocclusion it is always mandatory to ask the patient if his teeth mesh normally and feel normal. Often the only clinical evidence of the alveolar fracture is a loose tooth which "blocks" the occlusion. All teeth must be tested for first, second or third degree loosening. This is best done by forcefully manipulating each tooth between the thumb and index finger in the horizontal and vertical direction.

X-ray Examination

The physician should always specifically request "occlusal views of the mandible and maxilla" and intra-oral dental x-rays. Occlusal views give much more detailed information about the contour of the upper and lower alveolus and the position of the fractured teeth in relationship to the dental arch than do routine roentgenograms of the facial bones.

Examination of Nasal Cavity, Buccal Alveolar Sulcus, Lips and Floor of the Mouth and Tongue

Occasionally an empty socket, especially in the upper jaw, may indicate a more serious injury than one would suspect from a cursory examination of the maxillofacial region. If no root or crown fragments remain

in the socket or oral cavity or have not been found at the site of the accident, one should be suspicious that the missing teeth or their fragments may have been driven into the adjacent structures. The upper lip, the nasal cavity or the alveolar buccal sulcus may harbor the missing parts. Since they are all radiopaque, they can be traced by x-ray examination and should be removed before infection develops.

Treatment of Alveolar and Dental Injuries

The treatment of alveolar injuries is primarily aimed toward restoring the patient's exact pre-accident occlusion. It should be remembered that occasionally the pre-accident occlusion was not normal or ideal. For a large number of patients an "over- or cross-bite" represents normal occlusion. Secondly, attention should be directed toward preservation of the fractured teeth. This is especially important when the canine central incisors and first molars are involved, since these teeth are the most difficult ones to replace by prosthetic means. The last consideration should be given to the repair of the injury by prosthetic means.

Emergency Care

An adequate airway and the control of bleeding should be provided immediately. In the past the primary intention of protecting and securing an adequate airway often leads to a much too vigorous attack on loose teeth and alveolar bone fragments which were usually discarded or sent to the pathology laboratory as surgical specimens. This is no longer necessary nor in the best interest of the patient. If the injured tooth or root has reasonable support from the socket, great care should be used to preserve it. In the acute care, badly damaged teeth and bone may be saved by gentle manipulation and protective ligature anchorage to intact teeth. Only fractured crowns which are loosely attached to the gingiva and therefore represent a hazard of inspiration should be removed immediately, while fractured roots adequately embedded in the bony tissue must be preserved for possible future prosthetic foundations. In fact, all intact teeth and al-

veolar bone fragments which are so loose that they might represent aspiration problems should be removed in the emergency room and preserved in saline solution, to be reimplanted when definitive treatment is carried out.

Definitive Care

The closed or open reduction of the alveolar bone is usually combined with fixation of the teeth by means of wire loops and metallic or acrylic splints.

The fixation of a large alveolar segment hinged on the mucoperiosteum or one cortical layer can usually be done by closed approach with loop-wire support to solid neighbors or to a dentally fixed wire arch.

If the classical loop wire fixation is too traumatic or not possible, it can be avoided by protective splinting with quick setting acrylic or surgical cement.

Open reduction may occasionally be required when a large segment has been totally avulsed. This is done by placing stainless steel wire loops through the loose and solid segments.

Complications and Conclusions

Loss of the alveolar buccal sulcus can be

most disabling and can even make later denture preparation impossible without sulcus inlay skin graft. Therefore mucosal avulsions from the buccal alveolar sulcus require careful replacement and suturing. Stent support for several days may be helpful in maintaining the position of a flap. Teeth which suffer injury — be it only a concussive blow — should be assessed periodically for several years. Delayed pulp deterioration is not uncommon and should be diagnosed before tooth discoloration, infection or apical cystic resorption occur so that root canal filling can be done. The simplest diagnostic follow-up is the test for sensitivity with a spicule of ice. The patient can be instructed in this, or he can be periodically re-evaluated by his dentist.

Fracture of the alveolar segment of the mandible and maxilla is an important injury principally because of the teeth involved. Adequate and prompt treatment will restore the normal function of the teeth and a cosmetically and esthetically pleasing appearance. Mis-diagnosis and incorrect treatment, however, can result in irreparable loss of the alveolar bone and teeth together with severe occlusion and articulation problems.

Why Doesn't the Doctor Tell?

It is somewhat strange, that a class of men who can command such interesting, extensive, and instructive materials, as the experience of most members of the medical profession teems with, should have hitherto made so few contributions to the stock of polite and popular literature. The Bar, the Church, the Army, the Navy, and the Stage, have all of them spread the volumes of their secret history before the prying gaze of the public; while that of the Medical Profession has remained hitherto, with scarcely an exception, a sealed book. And yet there are no members of society whose pursuits lead them to listen more frequently to what has been exquisitely termed, The still, sad music of humanity.

— Samuel Warren (1807-1877)

Syphilis simulates every other disease. It is the only disease necessary to know. Know syphilis in all its manifestations and relations, and all other things clinical will be added to you. — Osler

Conscience: where there's a will, there's always a weigh. — Mary Dorsey

**Os
frontale**

**Sinus
frontalis**

**Crista
galli**

**Os
nasale**

Lamina cribrosa ossis ethmoidalis

Lamina perpendicularis ossis ethmoidalis

**Cellulae
ethmoidales**

Maxilla

**Os
lacrimale**

**Hiatus
maxillaris**

special formula for a special problem

*specifically formulated
for symptomatic
relief of sinus headache*

Sinus headache is not a single entity,
but a chain reaction of pain.
It is facial pain—deep, dull, aching and
nonpulsating. It is referred pain—
originating in the nose and sinuses but
felt at another site. It may become
generalized pain and tension in head and
neck. It is one or all of these.

The Sinutab formula is designed
for symptomatic relief of sinus headache.

It provides two analgesics to relieve
pain and discomfort...an effective oral
decongestant to reduce mucosal congestion...
and an antihistamine to help
control allergic manifestations.

Side Effects: Epigastric distress, drowsi-
ness, dizziness, insomnia and nervousness.

Precautions: Instruct patients not to drive
or operate machinery if drowsiness occurs.

Use with caution in patients with thyroid
disease, heart disease, hypertension, diabetes
or kidney disease. Excessive dosage or
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SINUTAB[®] for sinus headache

Each tablet contains
150 mg. acetaminophen,
150 mg. phenacetin,
25 mg. phenylpropanolamine HCl,
and 22 mg. phenyltoloxamine
citrate.

6-08-71-CC

**Sinus
sphenoidalis**

**Os
occipitale**

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Fractures of the Mandible

G. S. FITZ-HUGH, M.D.*
Charlottesville, Virginia

IN A WORKING classification of facial bony injuries, the less frequent ones involving the frontal sinuses are considered in the upper facial group; the midfacial, the more common, including those of the facial bones such as nasal, internal orbital floor, maxillozygomatic complex, maxillae, zygomatic arch, etc. are categorized as midfacial fractures, and those of the mandible, occurring almost as often as the midfacial group, as lower facial fractures.

The otolaryngologist in the management of midfacial injuries will often encounter fractures of the mandible as part of the multiple injury complex presented by the patient, usually as the result of an automobile accident. Or in the event no fracture of the mandible exists, he may find it advantageous to utilize this bone as a substantial, stable, fixed point which will be useful in the reduction and immobilization of severe midfacial fractures such as the Le Fort I, II, and III, and in the unilateral maxillozygomatic types.

Diagnosis

Fractures of the mandible are not difficult to diagnose, especially if one is aware of the fact that significant bony injuries may occur with minimal evidence exhibited in the overlying soft tissues. Supporting evidence of fracture includes: decreased and abnormal mobility of the lower jaw, localized areas of swelling, crepitation, salivation, etc. All fractures or suspected fractures of the mandible should obviously have radiographic examinations. Fracture of the symphysis, horizontal ramus and angle may be readily detected. Fractures of the condylar processes may be difficult to demonstrate and will require special techniques. It should be recalled that in the case of fractures of the lower jaw, the muscles of mastication will influence the

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position of the fragments. In contrast, there is no such action upon the fractures of the other facial bones. Fractures of the mandible are usually multiple, and those of the condylar area may be overlooked. Fracture displacements with dislocation of the condylar head from within the glenoid fossa are not as difficult a problem as one would anticipate. The occlusion of the first molar teeth in the upper and lower jaws may be used as the key for proper reduction of the fracture. It must be remembered, though, that in certain cases pre-traumatic malocclusion may have existed, and this should be considered physiologic and functional.

Treatment

Antibiotics

Antibacterial drug usage is indicated in fractures involving the tooth-bearing areas, as they will invariably be compounded intra-orally, thus creating an entrance for infection.



Fig. 1 — Winter dental arch splint mandibulomaxillary fixation. Craniomandibular and craniomaxillary suspension. Transosseous wiring.

X-Rays

In general, time should not be wasted in the emergency room struggling for definitive radiologic views of the facial bones in a case with multiple body injuries. Such films are better ordered later when more accurate ones can be had. In the case of a severe mandibular fracture displacement temporary support by wiring or a sling dressing may be useful in minimizing bleeding, edema and discomfort.

Closed Reduction

The vast majority of fractures of the mandible containing an adequate number of teeth may be managed by reduction and then immobilization, by placing the teeth of the lower jaw in centric occlusion against those of the upper jaw. First a prefabricated malleable metal arch splint of the Winter, Erich, or Jalenco types is fixed to the teeth of the upper dental arch with stainless steel wires (24 gauge). Next, after the mandibular fractured fragments are properly positioned, a similar splint is applied to the lower teeth. Then a separate segment of splint is applied to the teeth of each fracture segment. The procedure may be performed under general or local anesthesia. The splints contain hooks



Fig. 2 — Erich dental arch splint mandibulomaxillary immobilization for subcondylar fracture.

or lugs, and to these (after complete recovery from general anesthesia when used) elastic bands are placed between the upper and lower lugs in strategic positions in order to bring the teeth into proper position, thus reducing and immobilizing the fracture (Figure 1). Mandibulomaxillary or intermaxillary fixation is continued for a period of four to six weeks. This method of treatment was formerly considered a temporary one to be utilized only until more elaborate intra-oral appliances and prostheses could be prepared. Its success, however, has led to its use in the majority of cases as a permanent solution.

Open Reduction

In fractures of the edentulous mandible and in special situations where teeth are present, open reduction by the extra-oral or intra-oral approach is our first choice. This method is particularly applicable to fractures in uncooperative, mental, and alcoholic patients. Under general or local anesthesia, the fractured bone is exposed by the external or intra-oral approach (usually the

former). The fragments are perforated with a bone drill, care being taken to remain above or below the mandibular canal in order to protect its contents. The fragments are wired directly (trans-osseous) in proper position with stainless steel after reduction of the fracture. Mandibulomaxillary fixation is sometimes utilized as a supplement to the trans-osseous wire fixation.

Circumferential wiring of the mandible, using as a splint the patient's denture or a Gunning type of appliance, is effective in the immobilization of a fractured edentulous mandible in certain cases. Intramedullary wire fixation with a Kirschner pin may be utilized alone or as a supplement to other means in the management of a fractured mandible without teeth.

Immobilization of the Edentulous Fracture

Plastic headcaps for immobilization or suspension purposes are utilized very infrequently now, usually only in fracture of the edentulous mandible with bilateral subcondylar fractures. Under the best conditions, this treatment modality is uncomfortable and usually unsatisfactory. Extra-oral skeletal pins are now employed even more infrequently than the headcaps.

Condylar Fractures

Fractures involving the condyles of the mandible are interesting because they do so well with minimal treatment. They may be intracapsular or extracapsular (subcondylar). As the neck of the mandible is its weakest point and the glenoid fossa is quite solid, condylar fractures are common. If the condyle is displaced, bony contact is usually maintained within the capsule and periosteum. Healing in the malaligned position will result in no appreciable joint dysfunction. If actual dislocation from within the fossa occurs, fibrous pseudoarthrosis develops, and this is an acceptable sequela. Immobilization of the joint for a period of ten to fourteen days usually suffices to prevent a future painful joint or a "bite of convenience" (Dingman). Immobilization is accomplished by any one of the methods that have been previously mentioned (Figure 2).



Fig. 3 — Mandibulomaxillary immobilization which may be combined with transosseous wire fixation. Useful in children. Wires may be sheathed in polyethylene tubing.

Comment

What to do with the teeth damaged or undamaged in or adjacent to the fracture is a problem requiring individual consideration. Good teeth and those that may be useful for stabilization purposes should be retained if at all possible. Fractured teeth may be salvaged and restored to usefulness at a later date. Those teeth in the fracture line of a moderate to severely injured mandible are often extracted by the dental consultant.

Children

Fractures in children are rare compared to those in adults. This is mainly due to the lack of rigidity in the young and to the elasticity of the bone. When fractures do occur, however, they often present special problems. Deciduous teeth are unsatisfactory for the application of metal arch splints and mandibulomaxillary fixation. Open reduction with interosseous wiring becomes necessary. If immobilization of the entire mandible is necessary in the event of fractures involving the condyles, this may be accomplished by wires and elastic bands between the pyramidal aperture of the maxillae and mandible

(subcutaneous and intra-oral) as demonstrated (Figure 3).

Length of Fixation

The time factor in immobilization of mandibular fractures varies, depending upon the severity of the injury, the presence of teeth, and the age of the patient. Generally speaking, the maximum period of fixation should be six weeks and the minimum three weeks.

Acute dislocations of the temporomandibular joint are often spontaneous and not associated with trauma. The condyles are displaced anteriorly out of the glenoid fossae. If reduction is delayed an hour or so after sedatives have been administered, reversing the malposition by manual manipulation will readily reduce the dislocation.

Summary

Otolaryngologists have a primary interest in the management of upper and midfacial injuries. As fractures of the lower face (mandible) will often be a part of the injury complex, it is reasonable and necessary that they should be knowledgeable with regard to the management of such. In a general manner some of the problems associated with them are included in this brief presentation.

Babylonian Remedy for Gastric Complaint

If a man has stomach pain, let the man kneel on his feet and have burning juice of cassia poured over him, and he will recover. If *ditto*, let him kneel on his feet and let cold water flow over him. If *ditto*, place his head downwards and his feet up, strike his cheek forcibly, rub him violently, say to his stomach, "Be Good."*

*Rapport, Samuel and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 44.

The Doctor's Wife

I never walk out with my husband, but I hear the people bless him. I never go into a house of any degree, but I hear his praises, or see them in grateful eyes. I never lie down at night, but I know that in course of that day he has alleviated pain, and soothed some fellow-creature in the time of need. I know that from the beds of those who were past recovery, thanks have often, often gone up, in the last hour, for his patient ministrations. Is not this to be rich? The people even praise Me as the doctor's wife.

— Charles Dickens: Bleak House

We think our civilization near its meridian, but we are yet only at the cock-crowing and the morning star. — Emerson

Bell's Palsy and Post- Fracture Facial Paralysis

GEORGE E. SHAMBAUGH, JR., M.D.*
Chicago, Illinois

THE FACIAL NERVE is unique, having the longest course through a rigid bony canal of any nerve in the body. As a result this nerve is paralyzed more often than any other motor nerve in the human body. Ninety percent of cases of facial paralysis originate from disease occurring in the intratemporal course of this nerve (Cawthorne), only a small percent being of intracranial origin and about 5% due to a lesion distal to the stylomastoid foramen. Being nearly always the result of a lesion in its course through the temporal bone, a case of facial paralysis should first of all be considered an otological problem and should be referred to the otolaryngologist for diagnostic and prognostic studies. The reasons for such a referral will become evident as we consider the etiology and treatment of peripheral facial nerve paralyses.

Bell's Palsy

One hundred and fifty-six years ago, Charles Bell, anatomist and surgeon, read before the Royal Society of London an essay on the Nerves of the Face. That same year he was knighted for his neurophysiologic discoveries which included this essay in which he demonstrated the sensory innervation of the skin of the face by the *fifth* nerve, and the motor innervation of the muscles of expression by the *seventh* nerve. He proved his points by three cases of facial palsy following division of the seventh nerve at or near the stylomastoid foramen, one by a pistol ball, one by the horn of an ox, and the third due to extirpation of a parotid tumor: . . . "and the immediate effect has been the horrible distortion of the face by the prevalence of the muscles of the opposite side . . . and that distortion is unhappily increased when a pleasureable emotion should be reflected in the countenance." This vivid

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and picturesque description by Bell of seventh nerve paralysis has never been surpassed.

At first all cases of peripheral flaccid facial nerve paralysis were termed Bell's palsy, but as specific lesions occurring along its course were shown to involve the nerve by pressure, infiltration or trauma, the term Bell's palsy came to be applied only to those cases where no such external lesion could be demonstrated, and where the paralysis came on abruptly in an otherwise healthy individual.

Peripheral Facial Nerve Paralysis

Surgical Trauma

Among the specific lesions that can cause a flaccid peripheral facial weakness or complete paralysis, the most frequent is surgical trauma during an ear operation, with skull fracture involving the temporal bone gaining in frequency as the power and speed of automobiles continue to increase. Mastoid disease, especially cholesteatoma and carcinoma of the ear, are not rare causes for facial paralysis. Less common causes are glomus jugulare tumors, neurinoma of the facial nerve, acoustic neurinoma, and meningioma involving the temporal bone, all of them considered benign tumors, although glomus tumors and meningiomas are locally invasive and difficult to eradicate surgically. Facial paralysis is an early symptom of carcinoma of the outer or middle ear.

Idiopathic Facial Paralysis

The most frequent cause for peripheral flaccid facial paralysis is the idiopathic variety known today as Bell's palsy. The etiology and pathology are only partially understood. In 70% of cases a history of abnormal cooling of the mastoid region may be elicited, while 30% follow an emotional shock or abnormal stress. When the nerve is uncovered surgically within the first few months after onset a marked edema of it is observed, involving nearly always the vertical mastoid portion. Clearly, the paralysis has been the result of compression of the nerve in its rigid bony canal by this edema,

just as pressure upon any nerve blocks the transmission of nerve impulses, such as the familiar temporary loss of sensation in the hand when slept upon in a cramped position.

Bell's palsy recovers spontaneously and completely in the majority of cases, but in 15% to 25% of cases recovery is imperfect and incomplete, with spasm and synkinesis* combined with residual facial weakness, permanently marring the beauty of the features especially "when a pleasureable emotion should be reflected in the countenance." It is with this group of cases that the otologist should be concerned, since he can help to minimize the eventual deformity by timely release of pressure upon the nerve.

Pathologic Events in Bell's Palsy

The pathologic course of events in Bell's palsy is believed to be the following: local chilling or emotional shock causes an initial vasoconstriction, followed by venous congestion and edema. These same events in any other nerve will go unnoticed, but the facial nerve in the rigid confines of the fallopian canal becomes compressed by the edema, with blocking of electrical conductivity and nerve impulses.

The Effect of Pressure

The pressure, sufficient to block all nerve impulses, causes a damming up of axoplasm which continues to flow out from the parent cell body in the brain stem. As long as some axoplasm can squeeze by the compressed region the axon does not die, though it cannot transmit nerve impulses. If the pressure is sufficiently great the peripheral axon, entirely cut off from replenishment of axoplasm, will use up its axoplasm by catabolism, and will die. The result is then exactly the same as though the nerve had been sectioned. For a few days the distal end of the axon has continued electrical excitability as it continues to receive oxygen through the Schwann cells. Then its axoplasm begins to be used up by catabolism and begins to fragment with a gradual decline in electrical excitability. The myelin coating around the axon then fragments; but the Schwann cells, which are inde-

*See Test Your Word Score Page 1028.

pendent of the cell body of the neuron, remain, increase in size and number, and become phagocytic. They next proceed to engulf the axonal and myelin debris, and finally fill the connective tissue tubule of the nerve fiber. Meanwhile, the parent cell body and its nucleus, deprived of nutrients normally brought back to the cell through the axon, sickens, as shown by loss of Nissl substance and a swelling of the cytoplasm. Soon, however, a growth cone develops at the proximal end of the sectioned axon and begins a very active proliferation of protoplasmic processes and pinocytosis with taking in of nutrients that travel back in the axon to the cell body, which in turn becomes healthy again.

The Growth Cone

The growth cone of a young or regenerating axon can be studied in the living state by phase-contrast time-lapse cinematography. The sending out of protoplasmic processes seeking a favorable pathway for growth of the new axon results in branching, so that one regenerating axon often enters several neural tubules leading to widely separated muscle bundles. This accounts for the synkinesis always seen following regeneration of a severed or degenerated facial nerve. Some of the neural tubules will fill in with fibrous tissue closing them or reducing them in size before they are entered by a regenerating axon. The result will be failure of muscle fibers to be reinnervated, while other muscle fibers will be innervated by a very thin axon that remains unmyelinated and therefore uninsulated. This accounts for the muscle spasm and mass movement that follows regeneration of a facial nerve.

Surgical Decompression

The problem in each case of Bell's palsy is to determine when the pressure on the nerve is sufficient to begin causing axonal death and then to surgically decompress this early enough to relieve the pressure before many axons have died.

Optimum Time for Operation

Fortunately, the electrical excitability

test can indicate this. As long as the nerve on the paralyzed side shows normal excitability it is safe to temporize, but daily retest is indicated. As soon as this test shows progressive reduction in electrical excitability there is evidence that the pressure is sufficiently severe and prolonged to be causing axonal death, and prompt surgical decompression should be done. To wait an arbitrary two or three months and then decompress any case of complete Bell's palsy that fails to show beginning return of function is to wait until many or most of the axons are dead. On the other hand, surgical intervention *as soon as electrical excitability begins to decline* will be early enough to relieve pressure on the majority of axons while still alive so that they will recover without the permanent disfigurement of synkinesis, spasm, and incomplete reinnervation.

Exploration and Procedure after Fracture

Facial paralysis after skull fracture is due to edema, hemorrhage and often tearing or complete section of the nerve at the site of fracture. Just as Bell's palsy tends to recover spontaneously, so will many cases of facial paralysis recover after skull fracture, at least in part, without anything being done. However, the degree of and the chances for recovery are greatly improved by surgical exploration, decompression, and approximation of torn fragments in every case of facial paralysis that occurs immediately after a skull fracture. If the paralysis does not begin until a week or ten days after the fracture it is clearly due to edema and should be treated exactly like a Bell's palsy, with decompression only if and when electrical excitability begins to decline.

The facial trauma with marked edema of the structures that often accompanies skull fracture adds a diagnostic problem as to when the facial paralysis actually began. Not infrequently the facial paralysis is discovered only when the severe facial edema subsides. However, the more serious problems of cerebral concussion take precedence over facial nerve decompression, so that one may await the electrical excitability test results before deciding upon surgical ex-

ploration.

Summary

Bell's palsy and facial paralysis after skull fracture are otological problems:

First, because the site of lesion is within the temporal bone.

Second, because the decision as to whether or not to operate must be made by the otologist.

Third, because "all that palsies is not Bell's,"* and a careful otological examination is required to rule out other conditions that might be responsible for the paralysis.

Fourth, because surgical exploration of the fallopian canal and repair or decompression of the nerve requires the experienced otologic microsurgeon.

Finally, because the best chance of maximum recovery from Bell's palsy and facial paralysis after skull fracture requires timely surgical exploration and decompression or repair of selected cases.

*Cawthorne, Sir Terence.

First Use of Ether Anesthesia

In the National Statuary Hall in Washington, D. C., Dr. Crawford W. Long's statue bears the inscription: "Discoverer of the use of sulphuric ether as an anesthetic in surgery, on March 30, 1842, at Jefferson, Jackson County, Georgia."

Long had come to Jefferson to set up his practice in 1841, shortly after his graduation from medical school in Philadelphia. Soon thereafter, a "laughing gas" showman intrigued the townspeople of Jefferson with a lecture on the strange effects of nitrous oxide. Anxious to try the gas for themselves, several people asked Dr. Long for a sample. As it happened, the young doctor did not have any on hand but did have some ether, which, he assured them, would have about the same effect.

Some young men tried the ether in Long's office, became exhilarated, staggered about, laughed and behaved more or less as expected under the circumstances. But Long, more observant than most, noticed that as they staggered and stumbled about, bumping into furniture and bruising themselves, they seemed to feel no pain. Nor did he, himself, have any recollection of pain after joining the ether party and later finding bruises on his body. This set him to wondering about the possibilities of ether. If a small amount of it could mask pain of a bruise, would a larger amount be able to prevent the more extreme pain of surgery?

Dr. Long answered this question on March 30, 1842. James M. Venable, a participant in the ether experiments, had some tumors on his neck which he had delayed having removed because of his fear of pain. Long suggested that the use of ether might permit a painless operation. Venable agreed to its use. That night Dr. Long poured some ether on a towel and held it over the patient's nostrils until he fell asleep. When Venable awoke, he was astounded to learn that one of his tumors was gone. He had felt absolutely no pain during its removal. The first operation under ether anesthesia was a success and the fee, incidentally, was two dollars.

— Bernard Seeman: *Man Against Pain*

The doctor sees all the weakness of mankind, the lawyer all the wickedness, the theologian all the stupidity. — Schopenhauer

The Anatomy of the Lymphatics

Relationship
to
the
Dissemination
of
Malignancies
and
Infections

JOEL J. PRESSMAN, M.D.*
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OUR CONCEPT of the role of the lymphatics in the dissemination of cancer of the head and neck, as well as in the spread of infection, is undergoing rapid revision. This is due primarily to the observation that materials within the lymph nodes pass directly into the vascular system, in addition to escaping through the efferent lymphatic channels which previously had been considered the only outlet. As a matter of fact, the vascular route may be the far more important of the two, since lymph flow is sporadic and meagre, whereas blood flow is constant and rapid. The quantitative differences, however, have not been established for one route as over against the other. This newer concept not only seriously affects our interpretation of the physiology of the entire lymphatic system and negates many of the old established theories concerning it, but contributes greatly to our knowledge of the route of dissemination of cancer cells and bacteria.

Once looked upon as a trap or reservoir, which limited the spread of migrant cells and bacteria, the lymphatics can no longer be looked upon as fulfilling this role. As a matter of fact, the exact reverse may be the case; by serving as a breeding ground and periodically discharging their contents directly into the bloodstream, they may act as supplemental sources of infection or as sites for the spread of carcinoma. *Lancet*, commenting upon these observations, stated that these newer hypotheses seriously challenged Virchow's concept of an effective lymph node barrier as expounded in 1860 and held to be factual ever since.

Review of Literature

An old adage** says that upon discovering something new, one has only to look in the old German literature to find that it had

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**See Test Your Word Score Page 1028.

been discovered before. There has never been a better example than the subject under discussion. This supposedly new observation of a direct passageway directly from the lymph node to the vascular system, as it applies to both fluids and cells, was actually described in 1899 by Sigmond Von Schumaker in a paper entitled "Leukocytosis and the Efferent Paths of the Leukocytes in the Lymph Glands." Von Schumaker writes: "The smallest veins of the lymphatic substance present a peculiarity not only concerning their endothelial lining but also of another kind. It has been observed with extraordinary frequency that the vascular wall is penetrated by leukocytes . . . wholesale migration of leukocytes into the vessel walls rendered the latter to appear shredded in places and . . . passage of leukocytes from the lymph glands into blood vessels was observed. It seems likely, therefore, that direct migration of cells from the glands into the bloodstream took place." He then states that "the newly formed leukocytes in the lymph glands pass on their way to the bloodstream not by the longer route, via the thoracic duct, but by the much shorter one directly through the vessel wall," and suggests that "possibly the majority of leukocytes pass into the bloodstream from the lymph glands via the latter route." He then quotes Ribbert, who in 1890 wrote that "cells may pass from the lymph glands via the lymphatics into the blood or directly into the bloodstream. For more than 70 years, these observations remained relatively unknown, until it was our good fortune to rediscover them and once again bring them to light."

Migrating Tumor Cells

There are now numerous reports upon the presence of migrating tumor cells in the vascular system. It is likely these cells have passed from a primary site into the lymph node and directly from there into the bloodstream, most of them eventually being destroyed without establishing metastases. Parenthetically, this further suggests that a defense mechanism exists enabling the body to destroy cancer cells circulating into the bloodstream.

Our conclusions, as cited, resulted from experiments in which it was noted that air injected into a lymph node in conjunction with fluid passed directly and immediately into the bloodstream of the neighboring blood vessels and was seen simultaneously with the injection as bubbles in the bloodstream. We subsequently proved that this direct migration from the node to the vascular tree takes place in the instance of fluids as well and with cells the size of large bacteria; with the animals' own red blood cells and with Hela cancer cells. Having the advantage of modern advances in technology, our research techniques were more sophisticated than Von Schumaker's, particularly in the use of radioactive cells as tracers, but I am not certain that any evidence we have produced is more convincing than that Von Schumaker reported upon so many years ago. Many questions have been answered, as for example why the number and capacity of afferent channels to a node exceed those of the efferent channels and why lymphocytes do not disappear from the blood when all known lymphatic pathways are occluded by tying.

Practical Application

At the moment these observations seem to have little practical application to the everyday practice of medicine, except for the significance of one incidental observation which came about during the process of conducting these experiments. We believe it to be of the greatest practical importance. As has long been known, a lymph node discharges periodically into the efferent channel, and this discharge is increased by movements of the neck which increase pressures upon the node. The degree of pressure involved need not be greater than the physiological limits concerned with ordinary movements of the head and the contraction of the muscles of the region. Little has been written concerning the effect of pressure upon the emptying of an infected lymph node or one bearing malignant cells, and certainly little attention has been paid to this from the practical standpoint of everyday practice. This observation, however,

raises the question of the advisability of permitting large groups of students, for example, to palpate involved lymph nodes, thereby increasing intranodal pressure and possibly forcing the contents of the node into the vascular and lymph stream in large numbers. We have been equally concerned with the handling of lymph nodes in the course of surgical procedures. Definitive experiments carried out with this in mind have proven conclusively that during the course of surgical procedures upon the neck, a lymph node can be virtually emptied of its contents by pressure exerted upon it during the course of ordinary manipulations, this emptying taking place by escape through the efferent lymph channel, and the adjacent blood vessels as well. Using dyes, it was noted that the efferent channel distends notably as the result of minimal pressures upon the lymph node exerted by a palpating finger, and that cells not previously found in the bloodstream can be recovered from it during the course of such palpation and in greatly increased numbers in the efferent channel.

We have further observed that occlusion of the efferent channel can cause an escape of the contents of the lymph node. This raises the question of whether or not these untoward effects might not result from x-ray

therapy, biopsies, or excision of lymph nodes which destroy the escape routes, making the surgeon an innocent contributor to the dissemination of cancer beyond the node into the adjacent neighboring structures where, away from circulating fluids, they do not enjoy an equally good chance to encounter whatever protective measures the body provides and which are not as yet understood.

Our researches qualify as good research by reason of the fact that they ask more questions than they have answered. A larger number of workers now devoted to the study of the lymphatics will beyond all doubt provide some of the answers to the basic theoretical questions involved and, in so doing, provide answers to many questions of practical importance to all physicians concerned with the treatment of malignancies and infections, and for all those concerned with the lymphatic system in general.

Our present studies are concerned with electron-microscopic determinations of the micro-anatomy involved, since it is apparent that this interchange takes place as a result of the minute microscopic anatomy of the lymph node at the level of endothelial capillaries common to the lymphatic and blood vascular channels.

Remedies Derived from the Elm

The leaves, bark, and branches of the elm have the property of filling up wounds and knitting the flesh together: the inner membrane too, of the bark, and the leaves, steeped in vinegar, are applied topically for leprosy. The bark, in doses of one denarius, taken in one hemina of cold water, acts as a purgative upon the bowels, and is particularly useful for carrying off pituitous and aqueous humours. Many persons are of opinion that the bark of this tree, chewed, is a very useful application for wounds, and that the leaves, bruised and moistened with water, are good for gout. The moisture too that exudes from the pith of the tree, on an incision being made, applied to the head, causes the hair to grow and prevents it from falling off.

— Pliny

There are two kinds of leaders in the world — some are interested in the fleece, others in the flock. — O. A. Battista

I prefer a dream to an illusion. In a dream I know my eyes are closed; in an illusion I think they are open. — Comtesse Diane

The Management of Metastatic Cancer

In
the
Region
of
the
Head
and
Neck

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THE MANAGEMENT OF metastatic cancer in the region of the head and neck has evolved through the early and disastrous attempts at surgical control in the latter part of the nineteenth century, through three hopeful decades of the application of irradiation in the early part of the twentieth century, to the present status of a radical neck dissection alone or in conjunction with the primary cancer in the head and neck region. The basic biological facts of the behavior of cancer in the head and neck have given authenticity to this method of management. Approximately ninety per cent of the cases of cancer in Stage I-II are localized in a specific region of the head and neck. Failure of cure in these instances is essentially failure of control of the primary cancer or the regional cervical metastases. The successful application of an investment type of composite resection has proven to be one of the most important advances in the management of extensive cancers with obvious lymph-node involvement and supersedes all other types of treatment in a primary effort for cure.

The application of the elective radical neck dissection in the absence of gross metastasis requires considerable prudence; the size of the primary cancer, as well as the anaplastic and invasive characteristics and the metastatic potential of the primary cancer give some justification for the procedure. However, the general application of radical neck dissection has no justification in the management of all primary cancers in the region of the head and neck. The success of such radical neck dissection is borne out by an overall cure rate of approximately twenty-five per cent in cases with proven positive nodes.

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Bronchogenic Carcinoma

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THERE ARE FEW pathologic entities which have been as startling and as ominous as the increased incidence of bronchogenic carcinoma in this generation. From a condition of some medical rarity to the second most common cause of cancer death in men has been its course in the past 35 years. Aside from certain well known and documented exposures to inhalants of various types of radioactive carcinogens, the one factor that can be attributed to this alarming problem is its relation to cigarette smoking.

Diagnostic Bronchoscopy

The diagnosis of bronchogenic carcinoma rests on obtaining representative tissue or cells from which the pathologist can establish the presence of cancer cells and, when possible, the morphology of a tumor. This is the responsibility of the bronchoscopist, who in many instances is an otolaryngologist. In bronchogenic carcinoma this procedure is accomplished by direct vision biopsy, by fluoroscopically guided bronchoscopic forceps biopsy, by random bronchial biopsy, and by various techniques of bronchial washings. Random bronchial biopsy may include tissue from the bronchial wall and, on occasion, has established a diagnosis by direct intra-bronchial lung biopsy. Cytology collection techniques are made more productive by collecting sputum samples during the cough associated with the administration of the tracheobronchial anesthetic prior to a bronchoscopy and four additional samples immediately following bronchoscopy. Accuracy in regard to site of involvement is improved by collecting individual specimens from the separate sides or even the individual bronchial segments. For better recognition of the morphology, secretions collected directly in centrifuge tubes and subsequently completely processed in the same tube avoiding loss of tissue fragments further improves the "take."

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Preoperative Bronchoscopy

These numerous procedures to improve the pre-surgical accuracy of diagnosis have been used for many years. Nevertheless, some of them are unnecessarily complicated and tend to prolong the definitive preoperative diagnostic time. The ease and simplicity of exploratory thoracotomy justifiably made it more expedient, in certain instances, to bypass some of these steps. Recently, however, two new therapeutic procedures have re-emphasized the importance of these steps. The first is the therapeutic effectiveness of cobalt radiation and the second is the conservation of lung tissue through limited resection and sleeve anastomotic technics. Both depend on highly accurate pre- and post-irradiation biopsy, and thus to pre-surgical bronchoscopic evaluation of tumor involvement.

A careful preoperative bronchoscopic evaluation is essential to determine the nature of the tumor, its upward extent along the bronchial or tracheal wall, and the character of the bronchi distal to the tumor site.

Preoperative bronchoscopy and, occasionally bronchography, suggest the site of tumor invasion as well as the character of the bronchial pattern and lung tissue beyond.

Surgical Procedures

Most of the surgical procedures fall into one of five categories. (1) Tracheal sleeve: resection of a segment of trachea (three rings); direct anastomosis of the proximal and distal edges. (2) Right upper lobe sleeve: resection of the right upper lobe and right bronchus adjacent to the upper lobe orifice; anastomosis of the intermediate to the right main bronchus. (3) Left upper lobe sleeve: resection of the left upper lobe and left bronchus adjacent to the upper lobe orifice; anastomosis of the left lower lobe bronchus to the left main bronchus. (4) Left

lower lobe sleeve: resection of the left main and left upper lobe bronchi, removing the left lower lobe; anastomosis of the left upper lobe bronchus to the left main bronchus. (5) Pneumonectomy and sleeve: resection of the right lung, carina and distal trachea; anastomosis of the left main bronchus to the trachea.

Postoperative Bronchoscopy

Twenty-four hours after surgery, physical and x-ray findings are obtained to evaluate the patency of the sleeve. Bronchoscopic aspiration is performed if rales, an absence of breath sounds, dullness or atelectasis is demonstrated. Mucosal edema, an irregular, firm suture line, a kinked bronchus, or the presence of secretions that the patient cannot raise through the site of anastomosis are observed. These findings necessitate thorough aspiration of secretions and gentle dilatation of the anastomosis. Thereafter, bronchoscopic aspirations are repeated, daily if necessary, until the lumen remains adequate for drainage and aeration. After the first week, granulation tissue develops in some patients which requires forceps removal to maintain an adequate lumen. Sutures within the bronchial lumen are obvious from the first postoperative examination. Silk sutures, 4-0 or 5-0, have been used, the knots all tied extralumenally; but after the first week or two the knots and suture ends are found intralumenally when they may be cautiously removed with bronchoscopic forceps. Granulation tissue may continue to form until all visible sutures have been removed. There has been little or no such reaction with newer plastic suture materials. Eventual healing is accompanied by varying degrees of scar tissue stenosis that requires occasional bronchoscopic dilatation. If hemoptysis occurs, a bronchoscopic examination is made to determine if further sutures or granulations are present or if hemoptysis is an indication of recurrence.

*I sent my Soul through the Invisible,
Some letter of that After-life to spell:
And by and by my Soul return'd to me,
And answer'd "I Myself am Heav'n and Hell."*

— Omar Khayyam (?-1123)

Advanced Laryngeal and Laryngopharyngeal Cancer

Combined
X-ray
Therapy
and
Surgery

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SINCE BILLROTH performed the first laryngectomy in 1873, the treatment of cancer of the larynx has been influenced by a variety of concepts, purposes, and progressive developments concerned with improvement of results. The introduction of the fractional method of radiation by Coutard in the 1920s as a modality to treat laryngeal cancer made a second method of therapy available. Since then, both surgery and radiation have proved successful in varying degrees in the treatment of cancer of the larynx. The size and location of the lesion together with the presence or absence of metastases to cervical lymph nodes have been the decisive factors which have tested the effectiveness of both modalities. The treatment of cancer of the larynx has raised functional considerations, particularly in the form of radiation therapy, partial procedures and radical neck dissection. It has been our contention that patient survival should be the prime consideration, but question exists whether complete evidence is available for all decisions.

So far, surgery or radiation separately has yielded poor results for advanced laryngeal and laryngopharyngeal cancers, and these lesions still remain a challenge to the laryngologists. It is our belief that the best opportunity for survival can be obtained by combining radiation and surgery in a unified plan for the treatment of advanced laryngeal and laryngopharyngeal cancers and metastatic lymph nodes. Combined therapy must be regarded as an uncompromising single approach, and it should be emphasized that combined therapy is not the same as instituting surgery months later, after radiation therapy has failed. Under such circumstances, the surgeon is dealing with a new generation of cancer cells and with the later post-radiation problem of fibrosis and obliterative endarteritis which

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seriously affects healing. We should like to submit this form of combined x-ray therapy and surgery as an evolutionary development in the treatment of advanced laryngeal and laryngopharyngeal lesions.

Treatment at Mount Sinai

A specific program of combined radiation and surgical therapy for advanced carcinoma of the larynx and laryngopharynx was started in the Department of Otolaryngology at The Mount Sinai Hospital in 1958. Included in this program were patients who could be classified as Stage III as determined by the VIIth International Congress of Cancer. Reclassifying the 37 patients according to the criteria of The American Joint Committee on Cancer Staging and End Results Reporting, it was found that 19 belonged in Stage IV, nine in Stage III and nine in Stage II.

The treatment program is a predetermined plan which involves three phases. First, 5500 rads tumor dose of cobalt 60 is administered to the primary tumor and neck nodes via parallel opposed ports in five to six weeks. Second, there should be an inter-

val waiting period of three to six weeks after the end of therapy to allow the radiation reaction to subside. Third, the surgical procedure, consisting of wide-field laryngectomy, ipsilateral hemithyroidectomy and radical neck dissection is performed.

Results

In this report the statistics studied up to April 1, 1966, will be presented. Thirty-seven patients were treated, and 19 of 25 were living and free from disease for periods ranging from two to seven years (Table 1). The survival rate for two years was 76%, for three years 74%. The available literature indicates that the difference between the two and five-year survival rates of these cancers treated with radiation is only 10%. Since the expected survival rates of these advanced cancers treated with either radiation or surgery alone range from 10% to 40%, we believe that the combined therapy approach will at least double the survival figure for laryngeal and laryngopharyngeal cancer in the category indicated.

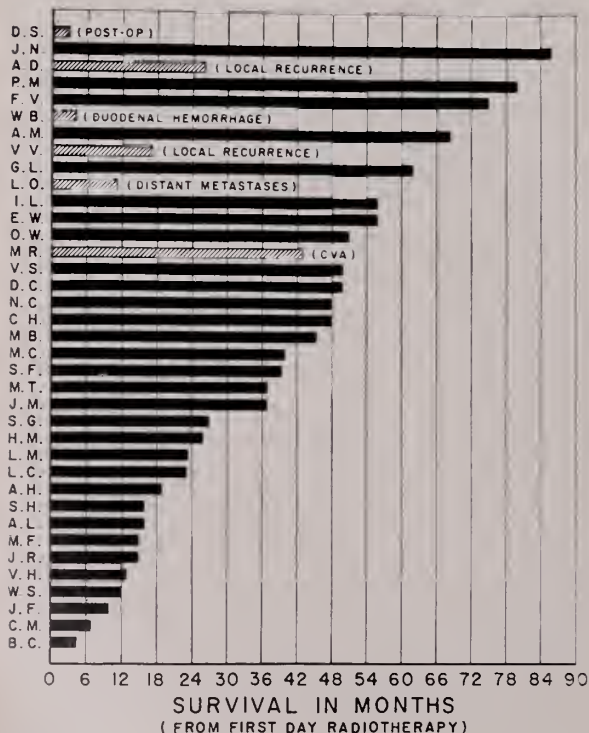
Examination of Specimens

As a result of the clinical effectiveness of this program, a histopathologic study of resected laryngeal and neck specimens was undertaken in 1961 in order to determine precisely the effect of radiation. We studied in detail, using en-bloc serial sections, the location of residual tumor nests and the manner in which cancer cells regressed and were destroyed.

Residual Tumor Nests

The size of the residual tumor nests that frequently were found in the larynges is of major importance. In five cases there were several tumor nests 0.5 millimeters or less in diameter. Two cases contained solitary tumor nodules between 0.8 and 1 millimeter in diameter. In the remaining larynx studied there was a single focus 1 × 1.5 centimeters in size. It became apparent then that in most cases the response to 5500 rads of teletherapy is such that the tumor regresses into tiny nests, distributed at random in the tumor bed.

TABLE



In the hands of many clinicians, teletherapy in the dose range of 5000-7000 rads is given as the primary treatment modality, and the patient is subjected to operation only if the lesion fails to respond to radiotherapy or if there is evidence of recurrence of neoplasm on mirror laryngoscopy some time after the end of the radiation treatment. It is our contention that the small size of the tumor remnants usually found after radiotherapy makes clinical evaluation of residual tumor very difficult or perhaps impossible for even the most experienced clinician. We also feel that the practice of doing random biopsies on an irradiated larynx carries with it only a small chance of finding these minute nests. We have seen cancer subjacent to intact mucous membrane both lying free in the subcutaneous tissues (Figure 1) and in the lymphatics. The most diligent follow-up examinations of these patients would fail to reveal the presence of these foci. These findings seriously question the practice of treating advanced cancer of the larynx with therapeutic levels

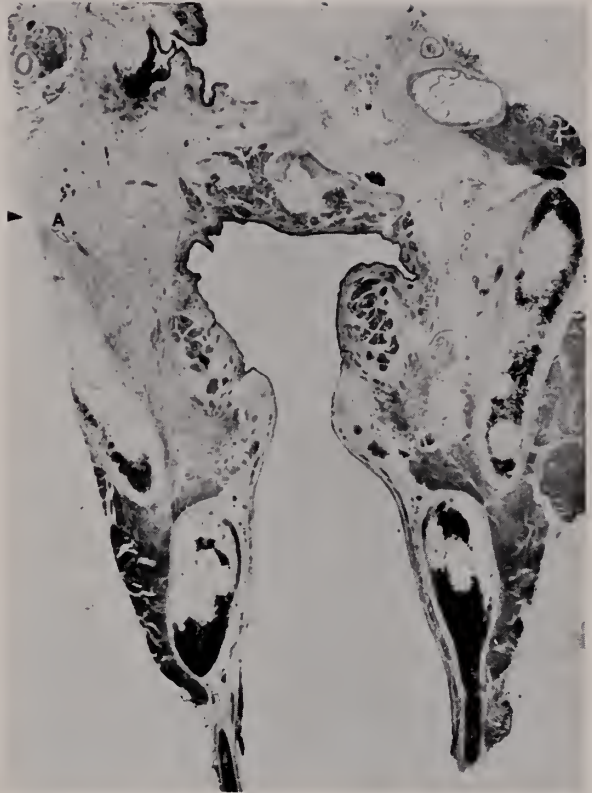


Fig. 2 — Nest of cancer cells (A) 1.5 cm. distant from mucosal surface.

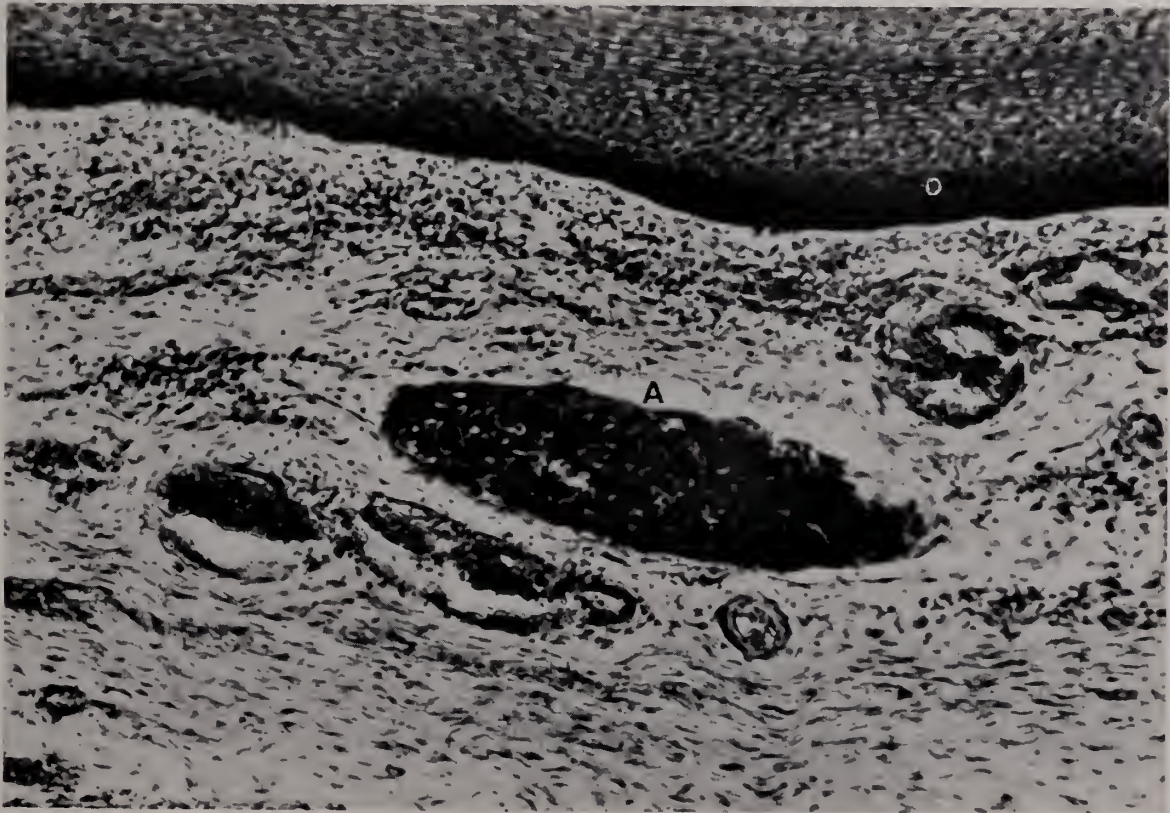


Fig. 1 — Cancer focus (A) in subcutaneous tissue beneath intact mucous membrane.

of radiation and operating only after the clinical appearance of residual carcinoma.

Another principle which has become clear as a result of our studies is that it is essential to remove the same volume of tissue which would have been excised if surgery had been the sole modality of treatment. If carcinoma were to undergo a centripetal regression as its response to therapeutic levels of irradiation, it would be possible to do a less extensive resection after radiotherapy. On the contrary, we have seen nests of tumor cells distant from the mucosal surface presumed to be the origin of the neoplasm (Figure 2). The locations of the residual cancer follow no discernible pattern and can lie anywhere in the area previously occupied by tumor.

Serial studies of irradiated neck specimens, inaugurated later in our program, promise to yield valuable information. Of three neck specimens which were considered positive before and after radiation, two were found to be free from cancer. In another specimen, all nodes palpable before radiation showed no evidence of cancer after radiation, but a small lymph node, four millimeters long, which was not palpated before radiation, exhibited cancer after radiation. It seems warranted to conclude that radiotherapy can in some cases sterilize cancer in cervical lymph nodes, even if the nodes remain palpable after treatment.

Discussion

The use of combined therapy for the treatment of cancer is not new. Our ideas were influenced by European laryngologists who advocated radiation therapy before and after surgery, the so-called sandwich method, for cancer of the larynx. However, we feel that the full benefit of a combined program cannot be realized by reducing the preoperative radiation by one half and radiating a large volume of tissue after surgery. It is our concept that the disease itself should be treated as thoroughly as possible before extirpation. Although preoperative radiation in the treatment of laryngeal cancer has not been used before in the way that we have

suggested, it has been employed in attacking cancer of the maxilla, lung, esophagus, endometrium, cervix, breast, colon, rectum and bladder.

It was natural that we were drawn to some form of combined therapy in view of our favorable experiences with radiation therapy for carcinoma of the larynx. The decision to use 5500 rads preoperatively was empiric, yet influenced by experience and carefully considered judgment. It was our desire to use a biologically effective radiotherapeutic dose which would not interfere with the performance of surgery. In general, it seemed reasonable that the largest effective dose that would permit satisfactory performance of the required surgery and produce the highest survival rate would be the method of choice.

The chief concern about preoperative radiation has been the anticipated influence on ensuing surgical procedures. Complications have been frequent in our series because of the influence of irradiated tissues, but even this consideration has been difficult to judge clearly on a comparative basis. It should be realized that we have treated very extensive laryngopharyngeal lesions which required wide resections and presented difficult closures; nevertheless, the end results have been much better than previously reported for advanced laryngeal and laryngopharyngeal lesions, and all complications have been successfully treated.

Another question which has been raised in relation to this program has been the possible removal of cured larynges and radical neck specimens. It has been established that a certain small percentage of laryngopharyngeal cancers can be cured by radiotherapy; thus inevitably there will be such cases in our series. It has been our contention that it is impossible to determine whether larynges or associated neck tissues are free from disease by visual examination, biopsy, or palpation, and this has been supported by our study. The success of the combined therapy plan to achieve improved total results depends on an uncompromising policy.

Life is the art of drawing sufficient conclusions from insufficient premises. — Samuel Butler

Neoplasia of the Parotid Gland

Surgical Management

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SURGICAL MANAGEMENT of parotid tumors, if it is to be considered adequate, should consist of the complete removal of the neoplastic disease with as little damage to adjacent normal structures as compatible with its accomplishment. Ideally, adequate excision has been accomplished when the excised neoplasm is surrounded completely by grossly normal appearing tissue at least 1 cm. thick. The extent to which this ideal can be attained, however, will be governed to an appreciable degree by the location of the tumor within the gland, its size, and the pathologic nature of the neoplasm.

Preoperative Evaluation

Physical Examination

Although malignant neoplasia of the parotid gland occurs less frequently than benign neoplasia, any tumor of this gland should be considered malignant until proved otherwise. Clinical examination may suggest that the neoplastic process is benign or malignant. The former is suggested by a slow rate of growth without associated pain, fixation, or facial paralysis, whereas more often a malignant process is associated with an increased growth rate, pain, fixation to adjacent structures, facial paralysis, and occasionally ulceration.

Special Studies

Diagnostic aids such as sialography and needle biopsy may be helpful in evaluating the pathologic process. Sialography often permits differentiation of neoplastic and inflammatory conditions of the parotid gland and, on occasion, may aid in distinguishing a benign from a malignant lesion. Needle biopsy may help in crystallizing an opinion concerning the nature of the pathologic process in doubtful cases. The interpretation of such biopsy material is difficult, however,

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and as a result precise identification of the pathologic process involving the gland may not be possible. Its greatest value probably is in differentiating chronic inflammatory disease simulating tumor formation from true neoplasia of the parotid gland.

Frozen Section Examination

The true nature of the neoplasm, however, cannot be ascertained until final histologic examination has been completed by a competent pathologist. For this reason, permission should be obtained from the patient before definitive surgical intervention is instituted to permit any procedure deemed by the surgeon necessary to eradicate the disease. Frozen section examination during the course of the operation is helpful in determining the nature of the neoplasm and the extent of the resection necessary to eliminate it. However, such examinations are not infallible. On occasion, the frozen section diagnosis may not be compatible with the surgeon's opinion of the tumor when that opinion is based on extensive surgical experience with neoplasia of the parotid gland. In such instances, it is probably wiser to depend upon the surgeon's experience rather than on the laboratory report.

Benign Tumors

Benign tumors of salivary gland origin are classified as mixed tumor, Warthin's tumor or papillary cystadenoma lymphomatosum, muco-epidermoid tumor, and adenoma. The mixed tumor is by far the most common tumor found in the parotid gland. Next in order of frequency are Warthin's tumor, muco-epidermoid tumor, and the varieties of adenomas.

Permanent paralysis of the face is the most dreaded complication of any operation upon the parotid gland. As a result, the neoplastic process may be inadequately removed when fear of producing a facial palsy plays a dominant role in the surgical management of such lesions. Yet this should not be so. The facial nerve lends itself admirably to the adequate surgical removal of benign neoplasms of the parotid gland, for it affords a plane of dissection which can be followed

so that the superficial lobe of the gland and any tumor contained therein can be removed intact. Since many benign neoplasms are situated in the superficial portion of the parotid gland, superficial lobectomy is the surgical procedure of choice for the management of such lesions. If the dissection is carefully performed, permanent paralysis of the face should not occur.

Deep Lobe Tumors

A tumor arising in the deep lobe of the parotid gland may pose problems in its removal because it is situated beneath the facial nerve. The superficial lobe of the gland must first be removed so that the relationship between the tumor and the facial nerve can be observed. If the tumor is small, it may be possible to mobilize the facial nerve sufficiently so that it may be retracted gently in one direction or another and the tumor thus removed intact without significant injury to the facial nerve. If this is not possible because of the size of the tumor, the mobilized branches of the facial nerve should be retracted in an appropriate direction and the segment of the nerve that prevents removal of the tumor sectioned. The continuity of the sectioned portion may then be reestablished by neurorrhaphy. Whenever possible, it is preferable to section those branches originating from the cervicofacial division of the facial nerve, as paralysis of the corner of the mouth or lower lip is much less distressing to a patient than is paralysis of the eyelids. Large tumors of the deep lobe may extend deeply into the pharyngomaxillary space. When this occurs, osteotomy of the body of the mandible may be necessary so that the surgical field can be enlarged sufficiently to permit the tumor to be delivered intact. If the continuity of the mandible is reestablished by wire sutures placed in a crisscross manner through drill holes on either side of the osteotomy, the patient will incur no appreciable disability.

On rare occasions, the facial nerve may become incorporated in recurrent mixed tumors. When this is found to be the case during operation, no attempt should be made to preserve the integrity of the nerve.

Rather, the recurrent tumor and that portion of the facial nerve incorporated in it should be excised so as to prevent contamination of the surgical field by tumor cells, which would occur if any attempt were made to remove the facial nerve from the substance of the tumor. The defect in the facial nerve can then be repaired by an autogenous nerve graft with subsequent improvement in the facial paralysis.

Malignant Tumors

The satisfactory management of malignant disease of the parotid gland is much more difficult than is that of benign tumors. Although the fundamental principles of surgical treatment are essentially the same for both benign and malignant neoplasia except that less attention is paid to preservation of the facial nerve when the tumor is malignant, difficult decisions must be made by the surgeon relative to the extent of the excision necessary to eradicate the disease when the tumor is malignant. Ideally, wide excision with sacrifice of the facial nerve is indicated in all cases. However, there is wide variation in the clinical behavior of the various types of malignant neoplastic disease involving the parotid gland and, to some extent, this influences the surgeon's decision as to whether the facial nerve in any particular instance should be preserved or sacrificed either in part or in its entirety. It should be realized, however, that the surgeon carries a heavy burden of responsibility when he preserves the facial nerve in the presence of a malignant tumor.

Malignant neoplasia of salivary gland origin may be classified as malignant mixed tumor, muco-epidermoid carcinoma, adenocarcinoma, epidermoid carcinoma, and undifferentiated carcinoma. The last three exhibit more of the stigmata of malignancy than do malignant mixed tumors or muco-epidermoid carcinoma.

Adenocarcinoma

Adenocarcinoma is the malignant neoplasm of the parotid gland most often encountered, and one of its variants, the

pseudoadenomatous basal cell carcinoma, carries a grave prognosis. This is because clinically it resembles a benign lesion in many instances and as a result is often inadequately removed. For this reason, when this tumor is suspected before operation, total parotidectomy with preservation of the facial nerve, when the latter is not involved in the malignant process, is the surgical treatment of choice. If the suspected diagnosis is confirmed by histologic examination, postoperative radiation therapy may be advisable, since evidence is accumulating that this tumor exhibits some degree of radiosensitivity.

The malignant nature of small tumors confined to the superficial lobe of the parotid gland may not be realized until the pathologic report has been received. Not infrequently, such malignant tumors have been adequately excised by superficial lobectomy. Under such circumstances nothing more need be done.

Facial Nerve

When exposure of the parotid gland reveals that it is involved in an infiltrative malignant process, even though facial palsy is absent, the lesion must be widely excised if a cure is to be expected. Under such circumstances the decision as to whether total parotidectomy should be combined with total or only partial sacrifice of the facial nerve will rest with the surgeon. Not all malignant tumors require complete sacrifice of the facial nerve. Malignant mixed tumors and muco-epidermoid carcinoma do not exhibit a high degree of malignancy as a rule and frequently can be adequately excised with resection of only that portion of the facial nerve involved in the tumor. However, when the malignant disease exhibits evidence of local invasion or lymphogenous spread manifested by preoperative facial paralysis and involvement of regional lymph nodes, more radical measures should be instituted. This involvement occurs most frequently with epidermoid and undifferentiated carcinoma of the parotid gland. In general, in such instances the operation should consist of total parotidectomy with sacrifice of

the facial nerve combined with radical resection of the cervical lymph nodes in continuity.

Discussion

Benign neoplasia of the parotid gland occurs with much greater frequency than does malignant disease. The surgical management of primary benign tumors of the parotid gland situated in the superficial lobe of the gland should pose no serious problems if they are completely removed at the initial operation. This is usually accomplished when superficial lobectomy has been performed. This procedure may not permit the inclusion of a border of normal parotid tissue on the medial aspect of a large tumor because the tumor capsule lies adjacent to the facial nerve. In benign encapsulated tumors, the facial nerve should be preserved unless the tumor is so situated in the deep lobe of the gland that section of a portion of the nerve is necessary to remove the tumor. The continuity of the sectioned nerve is then reestablished by neurorrhaphy.

Recurrent Tumors

Recurrent benign tumors pose a more difficult problem of management. Recurrence develops because initially the tumor was inadequately removed. As a result, the integrity of the facial nerve is placed in greater jeopardy when operating on recurrent tumors. Whenever compatible with adequate removal of the recurrent tumor, the facial nerve should be spared. If this is not possible, however, the portion of the facial nerve that prevents adequate removal should be excised and the continuity of the nerve reestablished by an autogenous nerve graft.

Immediate Nerve Graft

Although malignant neoplasia of the parotid gland occurs less frequently than does benign neoplasia, the management of malignant tumors is much more difficult and less satisfactory. The fundamental principle of adequate surgical excision still applies but, of necessity, less attention is paid to maintaining the integrity of the facial nerve. Sacrifice of the facial nerve is not necessary

in every instance for adequate excision of the malignant disease. When the facial nerve has been sacrificed to an extent that significant paralysis of the face results, it should be alleviated by autogenous nerve grafting rather than depending upon the hit-or-miss proposition that spontaneous recovery may occur.

Neck Dissection

When preoperative facial paralysis or cervical lymphadenopathy is indicative of local invasion and lymphogenous spread of the malignant process the surgeon has no alternative. In such instances, total parotidectomy, sacrifice of the facial nerve, and radical neck dissection are mandatory.

Radiation Therapy

The role of roentgen therapy in the management of malignant disease of the parotid gland has not been established. As the primary form of treatment for malignant neoplasia of the parotid gland of salivary gland origin, it has not proved as effective as has surgical intervention.

Surgical Judgment

The ideal treatment might be formulated but this does not mean that deviations from it necessarily indicate inadequate surgery has been performed or that the surgeon has not operated in the best interest of the patient. For example, diagnosis of a frozen section is helpful during surgical excision of a neoplasm in determining whether the tumor is benign or malignant and in obtaining adequate borders of excision. However, such diagnoses are not infallible. When the neoplastic process appears to be malignant in the judgment of the surgeon and the frozen section diagnosis indicates that it is benign, reliance is best placed on the surgeon's impression. In another instance, even though he realizes that residual tumor may be adherent to the facial nerve after the tumor has been excised, the surgeon may consider it more humane to forego sacrifice of the nerve in order that the patient may be spared the catastrophe of permanent paralysis of the face.

The Assessment of Vertigo

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VERTIGO OR DIZZINESS occurs when conflicting information from the sense organs, ordinarily concerned with balance, reaches consciousness. It is the resulting confusion which gives rise to the sensation of vertigo. The sensory mechanisms concerned with balance are visual, kinesthetic and labyrinthine. Adler (1941) has stated that ocular vertigo is never very severe. Cawthorne (1964) has made the statement that he has never seen a case of vertigo which could have been attributed to an ocular disorder.

Patients Description

Alpers (1941) stated that with central lesions, a patient's description of vertigo is vague and the patient finds it difficult, even with help, to define the nature of the sensations, whereas the patient with labyrinthine vertigo has no such difficulty. On the other hand, McNally and Stuart (1941) analysed the sensations which followed caloric stimulation of the labyrinth in a number of individuals. Many of the patients did not experience any sensation of rotation, and a large number of them did have difficulty in describing their sensation. Some said that it was a feeling of "going to faint," others a "swimming sensation"; yet others described it as a "weakness." A rotatory sensation may be the result of peripheral labyrinthine stimulation, but Alpers has found that it may also be present in lesions within the central nervous system.

Vertigo and Nystagmus

Jones (1918) pointed out that when rotatory vertigo results, following labyrinthine stimulation, the turning sensation is in the direction of the quick phase of nystagmus; whereas past-pointing and falling are in the direction of the slow phase.

In general, it is the nystagmus which is used as an index of labyrinthine reaction. On

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the other hand, Van Egmond, Groën and Jongkees (1948) stressed the importance of also recording the time of onset and duration of the after-turning sensations. The test which they named Cupulometry consists of minimal rotatory stimulation with recording of not only the nystagmus but also the after-turning sensations. It is still very much a laboratory, rather than a clinical, test.

Etiology

As to the cause of vertigo or its source of origin, Cawthorne (1957 and 1959) stated that in his personal experience of more than 2500 patients suffering from vertigo, the cause lay within the labyrinth or the peripheral vestibular neurons in 85% of cases and within the central nervous system in only 8%. He quoted Gower as having stated that in 106 consecutive cases of vertigo there were ear symptoms present in no less than 94% of the cases. Kase et al. (1965) report finding the complaint of dizziness in 820 of a series of 23,062 outpatients. In this series hypertension was present in 21.3% of the patients suffering from vertigo, and cerebral vascular disease in another 10.5%. They diagnosed Ménière's disease in only 8% of the cases.

Labyrinthine vs. Psychological

Labyrinthine vertigo is frequently associated with nausea and vomiting and there may or may not be headaches. Busis (1965) states that if nausea and vomiting precede the vertigo, or if vomiting occurs without nausea, the lesion is probably not of labyrinthine origin. If the vertigo is continuous, a functional etiology should be considered. Brain (1962), when discussing possible causes of vertigo, concludes with the following warning: "In all cases of giddiness (vertigo), however great the psychological factor, investigate the labyrinth; in all cases of giddiness, however great the organic factor, never forget the psychological reactions."

The association of deafness with vertigo suggests that the lesion may be in the peripheral end-organ, but this association does not exclude the possibility of central

nervous system disease.

Loss of Consciousness

The relationship of loss of consciousness to vertigo has led to a considerable amount of confusion and difference of opinion. In my experience, if there is a genuine loss of consciousness, a thorough neurological investigation has usually confirmed the presence of a central nervous system lesion. On the other hand, Riesco MacClure cites a case in his lecture series of 1958, in which there was vertigo with the patient losing consciousness for thirty minutes; yet the case is classified as one of bilateral Ménière's syndrome. It is hard to imagine how loss of consciousness can result from any lesion confined within the peripheral labyrinth.

Organic Disease

The occurrence of vertigo in the course of suppurative middle ear disease is of particular importance, because of the possibility that it indicates an imminent internal ear involvement.

When one is confronted with a patient complaining of vertigo, one should think of the general medical causes of such a symptom. Viral infection is regarded as a common cause but difficult to confirm. Vascular changes are probably the most common, such as arteriosclerotic changes in older persons, cardiac disease, vascular spasm in middle-aged individuals (I would say extremely common), small apoplectic central nervous system lesions, vertebral artery disease or compression of the vertebral artery due to cervical spinal disease.

Lesions

Above Entrance of Eighth Nerve

Lesions within the brain stem, particularly posterior-inferior cerebellar artery occlusion, must be considered. Carmichael, Dix and Hallpike (1965) have classified this latter lesion under two headings. They point out that the cochlear nuclei are all above the level of entrance of the eighth nerve, whereas the vestibular nuclei extend both above and below this level. If vertigo and

loss of hearing are prominent symptoms, this would suggest that the lesion is above the level of entrance of the eighth nerve; whereas, if there is no hearing loss, it would suggest that the lesion is below the level of the eighth nerve. For each of these areas they point out additional symptoms which help in localizing the lesion.

Lesions above the entrance of the eighth nerve are likely to be accompanied by abducens and facial paresis and widespread disturbance of trigeminal sensory function.

Below Entrance of Eighth Nerve

Lesions below this level are likely to give rise to disturbance of painful perception over the opposite half of the body and the territory of the first division of the ipsilateral fifth nerve, incoordination of the ipsilateral limbs, and paresis of the ipsilateral vocal cord and half of the soft palate. With still more caudal lesions there may be sensory changes in the ipsilateral upper limbs.

Miscellaneous Causes

More generalized central nervous system lesions, such as disseminated sclerosis, are also possible causes. Post-traumatic vertigo is a very well known phenomenon. Ophthalmological disease causing vertigo has already been mentioned. Biliary disease is a common cause of vertigo. The various drugs which can affect the labyrinth and cause vertigo, such as streptomycin, very readily come to mind as well as some of the other antibiotics such as Kanamycin.

Sensori-Neural vs. Cochleo-Vestibular Involvement

Hallpike and his group have stressed the importance of differentiating between the two more important types of sensori-neural, cochleo-vestibular involvement — the one being due to end-organ or hair-cell disease as in Ménière's disease and the other due to nerve fibre disease, as in eighth nerve tumor.

The fundamental finding common to both groups is bone conduction loss, and if the loss is unilateral, careful masking of the normal ear must be carried out.

End-organ Disease

In cases of end-organ disease, such as Ménière's disease, caloric responses may be normal between attacks, but they have been reported as abnormal in as many as 90% of cases by Carmichael, Dix and Hallpike. These latter found unilateral canal paresis, directional preponderance (which they ascribe to utricular disease), or a combination of both. They stated that spontaneous nystagmus is common during attacks, but that positional nystagmus is rare. These same workers have shown that the tests for hearing function are even more diagnostic in Ménière's disease than are the vestibular findings. There is usually a low tone sensori-neural fluctuating type of deafness. Speech discrimination is generally poor, loudness recruitment is always present, the Short Increment Sensitivity Index test is usually positive. Békésy audiometry tracings are usually Type I or Type II.

Nerve Fibre Disease

In the case of nerve fibre disease, such as in eighth nerve tumour, Carmichael et al. report finding abnormal vestibular reactions in 100% of their cases. According to them, positional nystagmus is rare. House (1964), reporting on his findings in early cases of eighth nerve tumour, states that if caloric reactions are normal it is very strong evidence that neither the labyrinth nor the vestibular nerve is the cause of the symptoms. He further emphasized that if there is involvement of the fifth and seventh nerves it is no longer an early case.

In nerve fibre disease, the sensori-neural hearing loss is typically of the high tone variety. Speech discrimination may be good or poor. Loudness recruitment is usually absent. The Short Increment Sensitivity Index test is as a rule poor. The Békésy audiometry may reveal tone decay as in Type III tracings, but Type II and Type IV tracings have been reported. House regards radiography in combination with radiopaque material as a most important diagnostic measure for early eighth nerve tumor.

The chapter on the diagnosis and treatment of acoustic neuroma will deal with the above matters in detail and will show how

House's translabyrinthine approach to the internal auditory meatus has emphasized the importance of early diagnosis.

Benign Paroxysmal Positional Nystagmus

Carmichael, Dix and Hallpike (1956) have classified another group of cases of possible end-organ disease under the term Benign Paroxysmal Positional Nystagmus. The term was first applied by Dix and Hallpike in 1952 to cases of vertigo which were found to show positional nystagmus — direction fixed and somewhat similar to Nylén's Type II. They consider these cases to be probably the result of otolithic disease. The caloric tests are often normal and there is frequently associated middle-ear disease, and in such cases there may be hearing loss.

The cause of the condition is thought to be trauma, low grade infection or vascular occlusion. Neurological abnormalities beyond the eighth nerve system are conspicuously absent. Some histological evidence has been put forward to support the idea that in these cases the lesion is in the utricle. However, Nylén has pointed out that in the histological evidence presented there were also lesions in other parts of the labyrinth and central nervous system. Some cases were reported in which destruction of one labyrinth eliminated the positional nystagmus.

However, Fernandez, Alzate and Lindsay (1959) found that a positional nystagmus which was present after a lesion in the nodulus of the cerebellum in cats, disappeared when the labyrinth on the same side was destroyed. This would indicate that disappearance of the positional nystagmus after labyrinthectomy does not prove that the causative lesion was confined to the peripheral end-organ in the above mentioned cases of Dix and Hallpike.

Vestibular Neuronitis

Carmichael, Dix and Hallpike have also described another group of cases in the nerve fibre disease class. To these cases they have given the term Vestibular Neuronitis. The vestibular reactions are abnormal in 100%. There is no positional nystagmus, and cochlear symptoms and signs are absent. The on-

set of the symptoms is frequently associated with infective illness. The clinical course is essentially benign. The pathological basis of this vestibular disorder still is a matter of conjecture. Because the galvanic test reactions were diminished in some cases it was thought that the neurons might be damaged. There is no histopathological evidence of a neuronal lesion.

Positional Nystagmus

The finding of positional nystagmus is important in a patient complaining of vertigo. Nylén has described two types — Type 1 which changes direction with alteration in the position of the head and is more common in central lesions, and Type II which has a fixed direction and may indicate either a central or a peripheral lesion. It is a modification of this latter type which Hallpike has described as benign paroxysmal and which has already been discussed.

It is important to note that positional nystagmus is an objective sign of organic disease which may be situated in the central or peripheral vestibular mechanism. Its diagnostic and lateralizing significance has not been uniformly accepted. These matters will be discussed in more detail under the heading of Postural Vertigo.

Directional Preponderance

The matter of directional preponderance has been much discussed in the literature. Under the term Nystagmus Bereitschaft, it was reported by Dusser de Barenne and de Kleyn (1923) and by de Kleyn and Versteegh (1927) as an indication of cerebral hemisphere disease. The term refers to a tendency for nystagmus to be more readily elicited towards one side than toward the other. Hallpike and his group changed the term to directional preponderance and reported that the phenomenon resulted from a lesion in the temporal lobe, but not from other parts of the cerebrum. Other workers have reported directional preponderance from other cerebral areas, and it has been reported in as high as 20% of normal individuals. De Kleyn and Versteegh (1933) reported directional preponderance in

Ménière's disease, and Fitzgerald and Hallpike (1942) reported its presence in Ménière's disease and in other labyrinthine lesions which they ascribed to the otoliths, especially to disease of the utricle. Hamersma (1957) believes that a directional preponderance is essentially a spontaneous nystagmus which has remained latent.

Jongkees and Philipszoon (1964) conclude from their study that in cases of Ménière's disease, postradical ear surgery, suppurative otitis media, brain tumours, the finding of spontaneous nystagmus, positional nystagmus and directional preponderance are not lateralizing diagnostic signs.

Electronystagmography

The possibility of making a nystagmogram or record of a patient's nystagmus has been a great step forward in the study and analysis of vertigo. Many important studies have been published which have contributed greatly to the interpretation of nystagmograms. It has been repeatedly emphasized that possibilities for misunderstanding and for outright error are many, unless each test is carried out with the utmost care being given to every detail.

Also, it has been stressed how important it is to record every single detail of the test on each particular occasion. The apparatus used must be described, eye movements must be calibrated, the electrodes must be positioned with great care (a loose connection will alter the record), the conditions under which the test is done — a relaxed or nervous patient, a drowsy or alert patient, a noisy or quiet room, a bright or darkened room, with eyes open or closed, with or without Frenzel's glasses: all these details must be noted.

The interpretation of the nystagmogram must be made by a physician skilled in otoneurology.

Recapitulation

The most important steps in the establishment of a diagnosis of the cause of vertigo are a thorough detailed history and a careful physical examination, both local and general.

The examination of the ears, nose and throat should be complete, including catheterization of the eustachian tubes. A thorough inspection of the ear drums should be made to exclude the possibility of a small perforation. If there is any evidence of middle ear suppuration, a fistula test should be done at the very first session of the examination to exclude the possibility of threatened internal ear involvement, as has already been mentioned.

An assessment of hearing should be carried out and, of course, vestibular examination must be carefully done.

Before doing any active stimulation of the labyrinth, too much emphasis cannot be laid upon the importance of a search for spontaneous phenomena, such as spontaneous nystagmus and especially for positional nystagmus. Unfortunately, one cannot be absolutely sure about spontaneous nystagmus until nystagmography with eyes closed has been carried out. Furthermore, as has already been mentioned, the significance of directional preponderance is even more doubtful until such information is available.

One should also look for cranial nerve involvement — e.g., corneal reflexes, etc., and for any sign of cerebellar disturbance.

The most readily applicable office test is some form of cold caloric stimulation of the ears. One of the simplest and yet quite satisfactory is cold air douching by means of a Dundas Grant coiled tube and ethyl chloride.

If any abnormality or asymmetry is detected, the more complicated alternate hot and cold caloric stimulation with nystagmography should be carried out. This latter examination is now available in most clinics, especially those associated with postgraduate teaching.

In this short review, treatment has not been considered. It must be stressed that medical treatment should be exhaustively tried before surgical treatment is recommended.

Because remission of symptoms is so common in many of the conditions causing vertigo, the possibility of a remission must be considered when assessing the value of any special therapeutic measure.

The Episodic Vertigoes

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THERE IS NO one whom the otologist would more delight to honor than M. Prosper Meniere.

He was the first physician, and an otologist, to attempt a more orderly classification of the vertigoes, which up to his day had been lumped under the classification of "congestive accidents of the brain."

Meniere's Disease

He called attention to a group of patients with episodic vertigo whose cardinal distinguishing feature was a bass type hearing loss in one ear. He also suggested that the origin of the hearing loss (and the associated vertigo) lay in the labyrinth of the affected ear, which made him the first physician to apply to clinical medicine lessons learned in the physiologic laboratory. This type of episodic vertigo was accordingly called Meniere's disease.

However, in 1917, G. E. Shambaugh, apparently owing to difficulty translating Meniere's papers, proposed the term Meniere's syndrome to cover all types of vertigo, whether intermittent or steadily attenuating and from whatever cause. No attention was paid to Meniere's cardinal sign of unilateral sensori-neural type hearing loss.

The introduction of the term Meniere's syndrome" into the American literature not only undid all that Meniere had hoped to accomplish by separating a specific kind of intermittent vertigo from the general group of vertigoes of intracranial origin but increased confusion by lumping together vertigoes and dizziness not of intracranial origin with those that were.

In spite of the fact that the dictionary defines syndrome as a group of symptoms that tend to occur together but may be of diverse origin, and defines disease as a group

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of symptoms and signs having a specific pathophysiologic origin, the term "Meniere's syndrome" rapidly gained popularity in the medical literature.

Meniere's syndrome and Meniere's disease are used as synonyms, and when this occurs the latter term becomes devoid of useful meaning. For this reason I believe that the term "Meniere's disease" should be abandoned in most instances and the term "the episodic vertigoes" substituted when a vertigo of short duration with a tendency toward intermittent recurrence is meant.

Episodic Vertigoes

If medical treatment is to be effective in controlling the symptoms of vertigo it must be directed at the cause. An etiologic diagnosis must at least be attempted.

Failure to obtain consistently favorable clinical results from treatment in the episodic vertigoes in all probability depends on the fact that having lumped them together under the term Meniere's syndrome, conditions of diverse etiology are subjected to a stereotyped method of treatment which in many instances should be considered illogical.

It must be granted, however, that differential diagnosis in the episodic vertigoes is rarely simple and easy, but rather is usually difficult and sometimes impossible by clinical examination or test.

Etiology

If this latter event proves to be the case it would seem reasonable to try to establish a working diagnosis of the etiology from the effects of various types of treatment.

It is illogical to follow too long a therapeutic approach which has proved disappointing. Another should be tried: one which may well be found effective on the basis of an etiology different from that primarily considered and subsequently found invalid.

If this plan is followed, most patients will receive such effective symptomatic relief from medical treatment that surgical intervention need never be considered.

There are many causes of intermittent

vertigo and many others which produce intermittent attacks of swimming in the head (or dizziness) which patients and many physicians confuse with vertigo.

Vertigo may be defined as an hallucination of motion of self or surrounding objects, while dizziness is defined as the sensation of something moving within the head.

Some of the conditions which might produce episodic vertigo are listed in the following table.

TABLE I
Causes of Episodic Vertigo
Otologic

1. Impacted cerumen.
2. Tubal occlusion with or without hypometabolic state.
3. Vasculitis involving internal auditory artery or vestibular emissary veins.
4. Hyper-irritable labyrinth.
5. Vertigo of labyrinthine destruction.
6. Post-traumatic vertigo (fracture or commotio labyrinthi)
7. Vestibular neuronitis.
8. Allergic reactions involving the labyrinth.
9. Senile degeneration of end organ.
10. Convulsive disorders involving the labyrinthine system (vestibular epilepsy, vertiginous epilepsy).
11. Migraine-like syndromes.
12. Meniere's disease.
13. Lermoyez's syndrome.
14. Sheehy's syndrome.
15. Ototoxic drugs.
16. Toxic effects and focal sensitization from infections of tonsils, adenoids, periapical tooth abscesses or sinuses.
17. Tumors of middle and inner ear.

Neurologic

1. Degenerating and demyelinating disease, especially multiple sclerosis.
2. Posterior fossa lesions.
 - a. Cystic arachnoiditis, syringobulbia, platybasia, Arnold-Chiari malformations, and fractures with involvement of substantia reticulata.
 - b. Neoplasms and subdural hematomas.
3. Supratentorial lesions with displacement of the brain stem.
4. Temporal lobe lesions with irritation of cortical areas.
5. Toxic infectious conditions.
 - a. Aseptic meningo-encephalitis.
 - b. Brain abscess.
 - c. Common viral diseases such as mumps, measles or whooping cough.
6. Vascular; including atherosclerosis, thrombosis, embolic occlusion and hemorrhage especially in fine vessels to the brain stem, the carotid and vertebral arteries.

Systemic

1. Cardiac disease.
2. Blood dyscrasias (anaemia, leukemia, lymphomas, polycythemia, purpura and reticulosis.)
3. Cogan's syndrome (non-syphilitic interstitial keratitis with vestibulo-cochlear symptoms — panvasculitis nodosa).

4. Hypertension (paroxysmal).
5. Hypotension (syncope).
6. Idiopathic paroxysmal hypoglycemia.
7. Cervical myalgia, arthritis and secondary fibrositis.
8. Addison's disease.

Ophthalmologic

1. Nonconcomitant strabismus.
2. Refractive errors.
3. Optokinetic vertigo.

Psychogenic

1. Tension — anxiety state.
2. Conversion reactions.
3. Neuroses (agoraphobia, claustrophobia).
4. Hyperventilation syndrome.

It would seem unreasonable to suppose that vertigo or dizziness arising from such diverse causes would respond to any single method of therapy, even if they were all categorized under the term "Meniere's syndrome" and the therapy was a centrally acting "antivertigo" drug.

Even if such medication gave symptomatic relief the physician would be derelict in his duty to his patient if he did not attempt an etiologic diagnosis.

Cervical Vertigo

Magnus pointed out that attitudinal reflexes are present in man and can be clearly seen under many pathological conditions.

Manifestations

It has been found, for instance, that the dysequilibrium of the inebriate is due to the fact that the attitudinal reflexes are depressed earlier and to a greater degree than the cortical functions by the ingestion of ethyl alcohol.

Magnus believed that the righting reflexes acted through reflex circuits to the utricular macula.

Travell described sudden vertiginous falling attacks which she believed acted through this mechanism. These seem to be similar, if not identical with the "utricular attacks" which Tumarkin ascribed to "Meniere's syndrome."

Gerlings observed that the head is often held to one side during an episode of "Meniere's syndrome" and suggested that the righting reflexes may sometimes be involved in this condition.

Cope and Ryan called attention to the fact that episodic vertigo may occur in cervical spondylosis and in cases of trauma involving the muscles and ligaments of the neck as in the so-called whiplash injury. It was their opinion that these lesions acted through the righting reflexes.

It would seem probable that a stimulus affecting the head or neck righting reflex is the most common cause of episodic vertigo.

Treatment

For episodic vertigo due to myalgia Travell found "trigger areas" in certain muscles, especially the sternomastoids. She found that spraying the tense muscle with ethyl chloride or injecting the relaxed muscle with a suitable anesthetic would abolish both the "trigger area" and the episodic vertigo.

In cervical episodic vertigo due to injuries to the cervical spine or ligaments Cope and Ryan stated that a well fitting cervical collar will give marked symptomatic relief.

Cervical traction has been highly recommended for cervical vertigo by some commentators.

Treatment should also be directed against the underlying or predisposing causes of cervical vertigo, such as hypoglycemia, ovarian dysfunction and the like.

Autonomic Dysfunction

Some observers believe that vertigo on the basis of autonomic dysfunction is the most common type. Mygind and Dederding pointed out that a great variety of autonomic stimuli might be reflected in stereotyped vascular reactions of a congenitally predisposed labyrinth. They found evidences of both vasodilation and vasoconstriction in the capillary beds of the labyrinth, neither seeming to predominate. It should be recalled that the autonomic nervous system does not produce vasomotion peripheral to the arteriole, the contractile elements of the metarteriole, precapillary sphincters and muscled venules being under autonomous control by vasoactive chemicals.

Manifestations

It would also seem proper to postulate autonomic stimuli to the fine vascular branches from the basilar artery which supply the longitudinal fasciculi and the vestibular nuclei as a cause of episodic vertigo.

The effect of such stimuli, in both labyrinth and brain stem, would be the production of intermittent vasospasm with anoxia, cellular injury, intravascular agglutination, increased vascular permeability, increase in interstitial fluid and release of toxic metabolites such as histamine, serotonin, or bradykinin.

Owing to the presence of vasoconstriction Davis suggested that it would be unreasonable to suppose that autonomic dysfunction affecting the labyrinth would result primarily in an endolymphatic hydrops as less, rather than more, endolymph should be secreted.

Seymour suggested that endolymphatic hydrops might result if a smaller quantity of an endolymph of increased osmotic pressure were secreted.

Vasodilators have been a popular remedy for intermittent vertigo on the presumed basis of autonomic dysfunction. Of the vasodilators mono-ethanol-amine-nicotinic acid appears to be the most effective in giving symptomatic relief. It has been found, however, that it is possible to achieve a considerably higher percentage of good therapeutic results if the intermittent vertiginous attacks are not associated with hearing loss but are of the type once characterized by Lindsay as "pseudo-Meniere's" disease.

Brunner reported that as a result of "vasomotor labyrinthitis" a hydrolabyrinth could be produced in which scala tympani and scala vestibuli showed equal or greater fluid accumulation than did scala media. He found that this condition might or might not result in the combined symptoms of pressure, tinnitus, deafness and vertigo. He was at a loss for an explanation of the variability of the symptoms.

Treatment

It is possible that this condition might be

related to failure of absorption of labyrinthine fluids and might be associated with cystic arachnoiditis of the cerebellopontine angle which some neurosurgeons have suggested to be a frequent cause of episodic vertigo with hearing loss. Drainage of the arachnoid sac has been reported to give long-term relief. It seems possible that the good results in "Meniere's syndrome" reported from the Portman-House procedure depend rather on relieving localized hypertension of cerebrospinal fluid rather than relieving hypertension of the endolymph.

Cogan's Syndrome

Manifestations

In a typical case of Cogan's syndrome the onset may be signaled by complaints referred to either the ears or the eyes. In some atypical examples of the condition, however, aural disorders predominate almost to the exclusion of eye symptoms.

It is interesting to note that the first case reported in the literature of a syndrome of non-syphilitic interstitial keratitis associated with vestibulo-auditory symptoms was reported as "Meniere's Disease Complicated by Recurring Interstitial Keratitis".

When Cogan identified this syndrome he included this case of Mogen and Baumgartner's as a typical example.

Cogan's syndrome is considered by most observers to be an instance of panvasculitis nodosa.

Many cases of Cogan's syndrome are difficult if not impossible to distinguish from "Rapidly Advancing Hearing Loss of the Younger Age Group" described by Sheehy. The hearing loss in both these conditions tends to be bilateral, with prolonged remissions, and further attacks are ushered in with a vertiginous episode.

It seems quite possible that Sheehy's syndrome and Cogan's syndrome may be closely related.

Treatment

In Cogan's syndrome glucocorticoid preparations are given in full dosage until a remission of symptoms had been obtained, and then cautiously reduced to a mainte-

nance dose, which must be continued for several months. This seems to give good results. The effect of this chemical in Sheehy's syndrome has not been reported.

Meniere's Disease

True Meniere's disease if selected according to the criteria suggested by the panel on vertigo of the National Institute of Neurologic Diseases and Blindness is a relatively rare condition not often seen even in a large outpatient service.

Manifestations

Since the hypotheses that Meniere's disease is caused by vasospasm, is untenable, as indicated by Davis. It has been suggested that the increased endolymphatic pressure is produced by the induction of histidine decarboxylase in a quantity far in excess of local homeostatic need, in a predisposed labyrinth, by stimuli arising from an ictal type of cellular "storm" in the hypothalamus. This would result in dilation of all vessels of the capillary beds of stria vascularis or the vas sperale below the basilar membrane with the secretion of an increased volume of endolymph.

Treatment

This hypothesis is supported by the fact

that eriodictyol glycoside in the form of lemon bioflavonoid complex has been found to suppress the symptoms of this condition.

Eriodictyol glycoside is one of the two bioflavonoids that Szent Györgyi found to have biologic activity.

Martin, Graff, Brendel and Beiler and Martin, Carley and Mok found eriodictyol and genesitin to be active in blocking histidine decarboxylase.

It is therefore considered probable that eriodictyol glycoside acts in Meniere's disease by blocking the activity of histidine decarboxylase.

Summary and Conclusion

Treatment of the episodic vertigos is not apt to be often successful if a single standard therapeutic program is applied to them under some meaningless cognomen such as "Meniere's syndrome."

It must be realized that intermittent stimulation of the labyrinthine system may result from a variety of causes. An etiologic diagnosis should be attempted. If this proves impossible, differentiation on the basis of the effect of treatment should be tried.

Post Hoc, Ergo Propter Hoc

The treatment of typhoid fever throughout the years has been variable and very interesting. An outstanding product used for a long period was antimony, which has no value in the treatment of the disease, but because it was given to Louis XIV and he seemed to improve following its administration, it became a favorite for years. Louis had been very ill with typhoid for a long time and showed no improvement with the usual concoctions of gold leaf suspended in wine, pearls dissolved in vinegar, and frequent poulticing. He was purged and bled, bled and purged and at last in desperation, his physician tried antimony. Louis was due to either die or get well and because the latter was in order, the antimony was given the credit.*

*F. William Saul, M.D.: *Pink Pills for Pale People*

Rosemary

Rosemary is a plant of great service in affections of the head and nerves, helping the apoplexy, palsy, and all kinds of convulsions, pains and dizziness of the head. It strengthens the sight and memory.

— Dr. James

Postural Vertigo

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DISORDERS OF THE vestibular system characterized by vertigo of the postural type have been recognized for nearly half a century, but in recent decades the clinical significance and the pathophysiologic basis for their occurrence have been the subject for considerable investigation.

Definition

Postural vertigo refers to vertigo which comes on only during certain postures. It may come on abruptly during a change into a certain posture, or it may have latency, appearing some seconds after the new posture has been reached.

Positional Nystagmus

The most useful objective indicator and confirming sign of the vestibular disturbance is the accompanying positional nystagmus. Since Bárány's first description of positional nystagmus in 1921,¹ considerable progress has been made in its clinical recognition, the method of testing, and the appraisal of its significance.

Localization of the point of origin within the vestibular system is, however, often indefinite, and the neural mechanisms involved in the release of the nystagmus have in most instances remained obscure.

History

The patient who complains of vertigo seldom volunteers the information that distinguishes "postural" from other types. A few well-directed questions will usually bring out the postural nature of the symptom and so permit the examiner to differentiate at least three common types of vestibular vertigo. These are: episodic vertigo with rapid onset and recovery such as in Meniere's disease, continuous prolonged vertigo following an acute onset such as a

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vascular lesion, and postural vertigo with or without a preceding acute onset of continuous vertigo. The patient with true postural vertigo usually gives a precise description of his symptoms in answer to a few selected questions. As in all cases of vertigo or disequilibrium, a general medical history is essential in the search for the cause of the disturbance.

Postural Tests

In addition to the routine ear, nose and throat examination the otoneurological investigation in all cases of vertigo should include routine postural tests. This should follow the tests for auditory function, disequilibrium, cerebellar function and spontaneous nystagmus, and it should precede the tests for vestibular function. Electro-nystagmographic recording of eye movements is useful in that it permits recording with the eyes closed and provides a record for later review. However, direct observation with the naked eye or with +20 diopter lenses or Frenzel's glasses to reduce fixation is adequate for clinical purposes.

Techniques

Two routines are in common use for changing postures. The simplest method consists of holding the patient's head slightly to the side between the examiner's hands and lowering it rapidly from the sitting to the supine position with neck extended. This is repeated with the head turned to the opposite side.

The more definitive method consists of using an orthopedic collar to prevent twisting of the neck, thereby preventing neck reflexes or alteration in vertebral vascular supply. Starting from the sitting position the routine may include supine, left lateral; supine, right lateral; supine, left sitting, then supine with collar removed and neck extended and rotated to each side in turn. Vertigo and nystagmus may occur during the change or may have a latent period; hence, 15 to 20 seconds are allowed before turning to a new position.

The test for positional nystagmus may in some instances depend on the rate at which

the posture is changed. Also the symptom may not be reproducible at the same examination.

Classification

Different classifications of the positional nystagmus have been used, mainly as an effort to evaluate its significance as to localization and etiology. The most commonly used is that which distinguishes three types based on its direction and duration.² One type is that in which the direction changes with the position or posture and is persistent. The second type is similar but the direction is always the same; while the third type includes a variety of transitory types, with or without latency.

Interpretation

The origin of the postural vertigo is best indicated by the associated findings, such as its association with a known inner-ear or retro-cochlear lesion or with indications of a central nervous system disturbance. Clinical observation has shown that the persistent types of positional nystagmus with or without vertigo are most suggestive of a central nervous system origin, whereas the transitory types may be of either peripheral or central origin.

Postural vertigo frequently follows an acute stage caused by partial lesions of the peripheral system³ such as viral labyrinthitis, vascular lesion with or without deafness, trauma during stapes surgery, ultrasonic therapy, and at times after an acute vertiginous attack in Meniere's disease. It also may occur in central nervous system lesions, including multiple sclerosis, tumor, vascular lesions and abscess. It is common following head injury, although localization may be obscure.

The transitory types are most common and their etiology often indefinite. They are frequently classed as "benign" since the vertigo is usually self-limited.

The term "benign" is questioned by some observers, since the "benign paroxysmal" type has been observed in cases of tumor of the posterior vermis⁴ and has been produced experimentally by cerebellar lesions includ-

ing the nodulus.⁵

Positional nystagmus has been produced experimentally by a variety of lesions of the peripheral vestibular system, including cutting the nerve to the utricle or to a semicircular canal.

Clinical Significance

Reliable evidence for a postural type of vertigo can usually be obtained by suitably chosen questions to the patient. Objective confirmation of its vestibular origin and organic nature can be obtained by observation of the positional nystagmus on postural

tests.

The presence of confirmed postural vertigo may be an early indication of progressive disease either of the peripheral or of the central nervous system; hence it is an indication for a complete otoneurological and medical evaluation.

Failure to recognize the postural character of the vertigo and to take steps to confirm its organic nature may result in dismissal of the complaint as purely psychogenic, or in overlooking an early sign of progressive disease.

References

1. Bárány, R.: Diagnose von Krankheitserscheinungen im Bereich des Oto-lithenapparates. *Acta Otolaryng* 2:434-437, 1921.
2. Aschan, G., Bergstedt, M., and Stahle, J.: Nystagmography. Recording of Nystagmus in Clinical Neuro-Otological Examination. *Acta Otolaryng Supp* 129, 1956.
3. Lindsay, J. R., and Hemenway, W. G.: Postural Vertigo due to Unilateral Sudden Partial Loss of Vestibular Function. *Ann Otol* 65:692, 1956.
4. Riesco MacClure, J. S.: Es el Vertigo Aural de Origen Exclusivamente Periferico. *Rev Otorrinolaring* 17:42, 1957.
5. Fernandez, C., Alzate, R., and Lindsay, J. R.: Experimental Observations on Postural Nystagmus in the Cat. *Ann Otol* 68:816, 1959 and Part II. Lesions of the Nodules. *Ann Otol* 69:1:94, 1960.

Ancient Greeks in Medicine

CELSUS (1st century A.D.) is notable for the description of inflammation, familiar to every medical student: redness, swelling, heat and pain (rubor et tumor, cum calore et dolore).*

ANTYLLUS (2nd or 3rd century A.D.) was the creator of arterial surgery, and was the first to distinguish aneurysm caused by pathological dilatation and aneurysm forming after trauma of the artery.

ARCHIGENES (98-117 A.D.) was one of the great surgeons of his era, operating in cancer of the breast and womb, and amputating limbs, with employment of the ligature, in a manner that we consider modern.

*Massengill, S. E.: A Sketch of Medicine and Pharmacy, The S. E. Massengill Co., Bristol Tenn.-Va.

Audio-Analgesia

Music to ease pain has been used for some time without any great scientific concentration on its possibilities. Today, a greater amount of attention is being focused on this particular area. Experiments are currently under way in which music and special static sound effects, known as "white sound", are played to a patient during certain types of dental or minor surgery. Preliminary results indicate that these combinations of relaxing music and somewhat disturbing white sound crowd the thalamus and cerebral cortex with a high level of sensory input and seem to reduce the sensation and recognition of pain.

— Bernard Seeman: Man Against Pain

|| Chemotherapy

in the Treatment of Head and Neck Cancer

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THE GREAT SEARCH for effective chemotherapy against cancer has been going on for the past ten years. Efforts have been directed at discovering new antitumor agents and in developing methods of administering them. It seems appropriate at this time to review the contributions of chemotherapy to the management of head and neck cancer.

Oncolytic Agents

Of the thousand possible oncolytic agents that have been investigated only a few have reached the stage of clinical trial, and a still smaller group have proved to be of clinical value. These are:

Alkylating Agents-

1. Nitrogen mustard (HN2, Mustargen)
2. TSPA or Thio-TEPA (Triethylene thiophosphoramidate)
3. PAM (phenylalanine mustard, Melphalan)
4. Cyclophosphamide, AB-100, TEM

Antibiotics-

1. Actinomycin D
2. Mitomycin C
3. Streptonigrin, dihydro E-73

Antimetabolites-

1. MTX (methotrexate)
2. 5-FU (5-fluorouracil)
3. FUDR (5-fluoro-2-deoxyuridine)
4. 8-azoguanine

Experience

The selection of an agent should ideally be based on the tumor's response to the agent when administered systemically. However, there is no way of determining this interaction, except by experience. The use of tissue culture has not proved to be of practical value in testing the effect of an agent on the specific tumor cells. Therefore, the choice of an agent is usually determined by the

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method of administration, as well as by the nature of the agent and the tumor response, as discovered by previous experience. Thus in perfusion techniques the short-acting alkylating agents are used, since the time of the perfusion is limited to one hour and the agent must destroy the tumor cells within that time. The treatment of melanomas of the head and neck is an example of the correct combination of administration and agent. Phenylalanine mustard, Melphalan, has been used most often in regional perfusion in melanomas of the head and neck. Nitrogen mustard, Triethylene thiophosphor and combinations of Triethylene thiophosphoramidate and phenylalanine mustard have also been employed and have been successful in producing total regression of the melanomas of the head and neck region. The alkylating agents have likewise been used successfully in the management of sarcomas. Favorable results have also been obtained with antitumor antibiotics given systemically. Embryonal rhabdomyosarcoma has been successfully controlled for a long period of time with a combination of agents, e.g., alkylating agents, antitumor agents and antimetabolites.

On the other hand, when antimetabolites are used, the exposure of the agent to the tumor must be continued over a longer period of time; for this reason continuous arterial infusion is the method employed. The two agents most commonly used are methotrexate and 5-fluorouracil. These agents have been most effective in the treatment of epidermoid carcinoma.

One should also mention hydrogen peroxide, which has been used by regional arterial infusion prior to and during radiation treatments. It is not an antitumor agent, however. This form of therapy is based on the enhancing effect of high oxygen content in the tissues during radiation. Objective evidence of this effect has been demonstrated in the reports of Mallams¹ and also of Corgill;² however, evidence that its long-term results are superior to radiation alone is still lacking.

The Administration of Antitumor Agents

Regional administration of agents is based

on the premise that the higher concentration of the agent in the tumor capillary bed will destroy tumor cells more effectively locally, while their dilution in the general circulation will spare the bone marrow and other vulnerable tissues. The two methods used are (1) regional arterial perfusion and (2) continuous regional infusion.

Regional Arterial Perfusion

In 1950 Klopp³ reported the use of nitrogen mustard by arterial perfusion in fractionated dosage in the treatment of cancer of the head and neck. Catheters were inserted into the external carotid artery. Bierman⁴ in 1951 reported the use of perfusion of nitrogen mustard, HN2, in the treatment of abdominal tumors. However, it was not until Creech⁵ in 1958 reported his results that regional perfusion began to be used extensively in the treatment of cancer. The rationale of this technique is to bring a high concentration of the oncolytic agent to the tumor bed while protecting the other vulnerable organs by isolation of the anatomic region from the general circulation. The agent is delivered into the arterial blood supply and picked up in the venous return, so that very little leaks into the general circulation. In the head and neck region the rich anastomosis makes complete isolation impossible, a serious limiting factor to the employment of perfusion techniques in the head and neck. The other factor is the narrow therapeutic index of alkylating agents, which are also toxic to normal tissues in the therapeutic concentrations used. A most serious complication of perfusion of the head and neck region is leakage of the alkylating agents into the internal carotid and the subsequent marked brain reaction and edema.

Creech⁵ used an extracorporeal pump and oxygenator. The trend has been toward simplification by elimination of the oxygenator and the use of a hand pump. Golomb⁶ has used this system as an adjunct to surgery. The tumor bearing area is perfused prior to its removal at the time of surgery. Harrison⁷ has also employed perfusion at the time of surgery, followed by radical excision of the tumor bearing area.

Regional Arterial Infusion

Sullivan and his colleagues⁸ in 1959 reported on the use of continuous arterial infusion for the treatment of tumors. Polyethylene catheters were inserted into the external carotid arteries for the treatment of malignancies of the head and neck. The anti-tumor agent methotrexate (MTX) is delivered continuously in high dosage (50 mg/24 hours) over a long period of time, usually ten days. No attempt is made to prevent the agent from entering into the general circulation. Protection of other vulnerable organs is accomplished by intramuscular injection of citrovorum factor (6 to 9 mg. every four to six hours).

The rationale of this method is based on three factors: (1) that cells are vulnerable to the antimetabolites only during the active phase of cell division, (2) that populations of tumor cells go into cell division stage at different times, and (3) that by infusion the antimetabolites are constantly present in the tumor bed in high concentration.

Methotrexate (MTX) has been most widely used following the technique of Sullivan.⁹ Johnson, Kiskin and Curreri¹⁰ have used 5-fluorouracil by continuous arterial infusion in a variety of tumors and followed this in three to four weeks either with surgery or radiation therapy whenever possible. As with most reports on chemotherapy both groups of investigators find that the number of immediate responses is encouraging, as are the preliminary recurrence and survival data in a group of patients with far advanced carcinomas of the oral cavity and pharynx.

Infusion remains the principal method of administering antitumor drugs in the treatment of head and neck malignancies. Many technical improvements have been added, including the insertion of catheters through the superficial temporal artery, improvements in the catheters themselves, and the simplification of the pump. The improvements help to solve the technical difficulties and reduce complications but do not alter the overall response of the tumor to the agent.

At the same time the procedure of perfusion has become more complicated. Boy-

land¹¹ has shown that nitrogen mustard is less toxic to the whole body when systemic hyperthermia is maintained during its administration. Shingleton¹² has also demonstrated that bone marrow is protected during hypothermia. Harrison⁷ has added hypothermia to his regimen. He pointedly remarks that perfusion with hypothermia for the body and hyperthermia for the regional perfusion has now become so complicated that it should be carried out only in a center for chemotherapy with a trained staff and with special facilities for the management of the patient and the complications. This is very sound advice for any form of chemotherapy.

Complications

There are several factors which limit the general use of tumor chemotherapy. These include the local and systemic effects on normal tissues, the technical difficulties of inserting catheters into the arterial system and maintaining their function, and the complications which arise from these procedures. The latter include hemorrhage, sepsis, vascular spasm, necrotizing arteritis, emboli formation, and thrombosis of the vessels. Transient and permanent hemiplegia is not an uncommon sequela. Reports of transient hemiplegia vary from 8 to 30%.

Combined Chemotherapy Regimens

Chemotherapy rarely produces a cure even when total regression of the tumor takes place. Biopsy specimens from the tumor site have viable tumor cells present. For this reason chemotherapy is now frequently used as an adjunct to surgery or radiation. Thus, perfusion of the isolated or semi-isolated tumor bearing area with an alkylating agent at the time of surgery has been employed by several surgeons. Harrison⁷ widely removes the perfused tumor tissue immediately after perfusion in order to forestall necrosis, sepsis and hemorrhage which might follow the destruction of the tumor. Johnson et al.¹⁰ have resected the tumor area three to four weeks after successful regression of the tumor or have used radiation therapy at this time.

Because of the complications arising from arterial infusion of the tumor site, Daly and Friedman¹³ have employed methotrexate (MTX) 7.5 mg. daily by mouth for ten days, in combination with radiation therapy. Their results are similar to those obtained by continuous infusion. Ten percent of the patients showed complete to near complete regression of the tumor on oral MTX prior to the start of radiation; two thirds showed fifty percent shrinkage, and fifteen percent showed no response. Radiation was added to the course of methotrexate. Oral methotrexate appeared to enhance the effect of radiation on the tumor. The authors express their enthusiasm for the encouraging results, but admit that a controlled study is needed to prove enhancement.

Results

Since antitumor chemotherapy rarely if ever produces a cure, its principal value lies in its ability to control the disease by producing a temporary regression of the tumor and an amelioration of symptoms. Reports in the literature are enthusiastic and hopeful but lack objective criteria for judging the over-all effect of the therapy on the course of the disease. Its palliative effects are real but temporary, recurrence within three months or less being the general rule. For this reason most investigators are combining chemotherapy with the two well established modes of cancer therapy, namely, surgery and radiation. To establish statistically an enhancing effect on the cure rate of five to

ten percent presents a formidable task, requiring the cooperation of a large number of clinics. Prospects for this type of study do not seem to be feasible, although some are already courageously trying to organize a national study of combined chemotherapy and radiation.

Conclusion

Antitumor chemotherapy by regional arterial administration is capable of producing a temporary control of the disease as judged by gross regression of the tumor and palliation of symptoms. Reports indicate that chemotherapy may enhance the cure rate of surgery and radiation when used in combination, but we do not have a controlled study to prove it. Local and systemic toxic effects and the complications from the arterial method of administration are factors which limit its general use. Oral methotrexate in combination with radiation therapy will produce a regression of the tumor, may enhance the cure rate in far advanced disease and is worthy of a trial. However, all precautions should be followed to avoid the systemic toxic effects of these lethal agents. Finally, the seriousness of the complications arising from the use of chemotherapy, plus the fact that chemotherapy is still in an experimental and developmental stage, makes it desirable to establish a tumor chemotherapy unit within a hospital complex where special equipment and personnel familiar with its problems may function to the benefit of the patient.

References

1. Mallams, J. T., Finney, J. W., and Balla, G. A.: The Use of Hydrogen Peroxide as a Source of Oxygen in Regional Intra-arterial Infusion System. *Southern Med J* 55:230, 1962.
2. Corgill, D. A.: Arterial Anticancer Drug Infusion Therapy. *Laryngoscope* 72:1158, 1962.
3. Klopp, C. T., et al.: Fractionated Intra-arterial Cancer Chemotherapy with Methyl Histamine Hydrochloride. Preliminary Report. *Ann Surg* 132:811, 1950.
4. Bierman, et al.: Intra-arterial Catheterization of Viscera in Man. *Amer J Roentgen* 66:555, 1951.
5. Creech, O., Jr., Krementz, E. T., Ryan, R. F., and Winblad, J. N.: Regional Perfusion Utilizing an Extracorporeal Circuit. *Ann Surg* 148:616, 1958.
6. Golomb, F. M., et al.: A Simplified Technic for Regional Perfusion. Report of Its Use in a Series of Twenty-Three Cases of Malignancies of the Head and Neck. *Amer J Surg* 102:839, 1961.
7. Harrison, D. F. N.: Clinical Experience of Chemotherapy. A Study of 100 Cases of Advanced Head and Neck Cancer. *Arch Otolaryng* 81:2, 1965.
- 8-13. May be secured from the author or the reprints.

The soul's maladies have their relapses like the body's. What we take for a cure is often just a momentary rally or a new form of the disease. — La Rochefoucauld

Intranasal Medication

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MEDICAMENTS, FOR a number of years, have been packed, sprayed and instilled into the nasal cavities by physicians in their treatment of various ailments of the nose and sinuses. Throughout most of this time, their efforts have been directed largely toward alleviating symptoms, rather than toward eliminating the conditions or disease causing the symptoms. Intranasal medications have been used in the management of the common cold, acute nasal and sinus infections, vasomotor disturbances, acute and perennial allergy upsets, longstanding head colds, atrophic rhinitis, chronic sinusitis, and various aches and pains about the head and face. It is, however, the opinion of most rhinologists that, with slight exception, little is to be gained by the use of most of the methods of intranasal medication.

Historical Items

In the early days, prominently displayed in most physicians' offices, was an array of spray bottles, containing oily solutions of different colors and aromas. The patient inhaled these, either in rotation or in accordance with the physician's mood and, as far as is known, no benefit was ever derived from their use.

Some time later the spray bottles were replaced by tamponage therapy with argyrol packs** which were inserted into the nose for twenty to thirty minutes. This was often repeated daily.

These packs in the nose are harmful in the acute stages and of no curative value in the chronic stage. In subacute infections, their irritating action produces a flow of mucus which some think of value. The same effect, however, can be attained by a few whiffs of snuff and with less damage to the nasal mucosa. The principal objection to the use of argyrol packs is that physicians,

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**Dowling packs.

who commonly use this method apply it to all patients with nasal complaints regardless of the nature of the ailment, are prone to develop loose diagnostic habits.

Shrinking nose drops came along a few years after Chen introduced ephedrine to occidental medicine in 1926. Ephedrine is an alkaloid derived from Ma Huang, known to the Chinese for many years as an anti-asthmatic and diaphoretic. The physiologic effects of ephedrine are principally due to its stimulating action on the sympathetic nerve endings in the nasal mucosa which produces nasal vasoconstriction.

Decongestant nose drops were welcomed by rhinologists and represented a period of enlightenment founded on what Proetz called the "rediscovery of the cilia."¹⁻⁵

Research initiated then and during the ensuing years aroused an interest not only in the ciliated mucosa but in all phases of nasal physiology with the result that much of the confusion previously existing in rhinology has been dispelled.

We know now that the membranes which line the nasal and sinus cavities are ciliated and covered with a thin layer of mucus in which the cilia beat. The mucociliary mechanism with its sticky surface guards against invasion of the tissues by pathogenic organisms, which are conveyed to the nasopharynx promptly; and only in the event of a breakdown in the mucociliary stream do the pathogens gain a foothold in nasal membranes.

By far the most common means of disrupting this defense mechanism is body chilling. This produces intranasal vasoconstriction, with lowered temperature and a blanching of the membranes which cover the intranasal structures. As the circulation is diminished, there is a cessation of glandular activity; the nose becomes dry and the cilia cease to beat.

A return of intranasal function will occur with the application of heat, either locally or to the periphery; or, if the individual's resistance is good, a compensatory action re-establishes nasal function in ten to twenty minutes in spite of continued exposure to cold.

Acute Nasal Infection (Common Cold)

It is a generally accepted belief at the present time that the micro-organisms usually associated with diseases of the upper respiratory tract have nothing whatever to do with the onset of the attack. They are secondary invaders only, coming on after the way has been paved by some other influence.

The early invader is thought to be a filterable virus which confines its activities to the initial stages of the disease.⁶

Just what part the virus plays in the onset of a cold is purely conjectural. Some investigators think the viruses pass through the ducts of the goblet cells and mucous glands; others think that in order to be available at the proper time the viruses must reside in the nasal mucosa of cold-susceptible individuals. The goal of many of the virologists at the present time is the development of a vaccine capable of establishing an immunity in human individuals. It is thought that success in this project is contingent upon development of a vaccine against a sufficient number of the specific viruses now known to exist.

General Management

Bed Rest and Moist Air

All writers agree that patients with acute rhino-sinusitis do better when put to bed in a warm, well-moistened room, and that simple common-sense treatment hastens recovery and prevents complications. Energetic local treatment is avoided, but measures to increase the comfort of the patient are introduced early and maintained throughout the course of the disease.

Local Heat

Important to the patient is the application of heat to the face. This may be in the form of hot moist towels or infra-red rays and are especially welcome during the engorged state of the nasal membranes.

Nasal Pack

For those complaining of excessive con-

gestion and pain, a soothing nasal pack also is indicated. This consists of cotton saturated with equal parts of ephedrine (0.5 per cent) and pontocaine hydrochloride (0.5 per cent). This is gently inserted into the nose in the area of the middle meatus and left in place for thirty minutes while the patient is also receiving external heat. With the removal of the packs the pain and congestion disappear, and this relief may remain for hours.

The shrinking effect of ephedrine on the swollen nasal membranes of an acute head cold affords immeasurable relief, yet its excessive use is discouraged, for its benefits must be weighed against the detrimental effects of the application which removes protective hyperemia of the nasal tissues, lowers local resistance and violates the principles of acute inflammations.

To be deplored is that practice of many physicians today who prescribe shrinking nose drops for the complaint of impaired nasal breathing without first seeking the cause and nature of the blockage. Even though a diagnosis has been reached, vasoconstrictors should be prescribed only with the understanding that very little of a curative nature may be credited to them and that the relief afforded will be temporary only. It should also be kept in mind that the continued use of nasal vasoconstrictors may lead to disturbances of nasal function to such an extent that allergic conditions remain neglected or uncontrolled and pathologic membranes may progress to a state of chronicity.

Rhinitis Medicamentosa

This title has been applied to the condition of the nasal mucous membranes which results from overuse of shrinking solutions in the nose. The mucosa covering the intranasal structures becomes pale and edematous. The swelling is sufficient to block the nasal airways and the condition persists except when a temporary respite is gained by a further application of a nasal decongestant. This form of rhinitis may be produced by the continued application of almost any of the vasoconstrictors in common use but

has especially been noted following the use of privity hydrochloride, a drug recognized for its prompt, pressor action.

Illustrative Case

A pronounced case seen by the writer a few years ago is typical of those cases occasionally encountered by all rhinologists.



Figure
Head in low positions for intranasal medication and displacement (suction) therapy. (Top) The Proetz position. (Bottom) The side position of Parkinson.*

*Postgraduate Medicine, November, 1963, p. 474.

Mr. D. had been using privity steadily, for three years as often as every two hours, day and night. Examination revealed pale, boggy nasal mucous membranes which completely blocked both nares. Pus was observed in the middle meati and irrigation brought a return of considerable pale exudate from both antra. He immediately stopped the use of all nose drops; but to aid him in sleeping with a blocked nose he was given phenobarbital each night for five nights and reported that on the sixth day his nose opened up satisfactorily. He was given dust extract injections in a dilution of 1 to 100,000 each week, and at the time of the injections the sinuses were irrigated. The sinuses were negative on the sixth irrigation and have remained so since then; now he no longer has the complaint of nasal stuffiness.

Nose drops employed in office practice are indispensable. As a shrinking agent to permit better visualization of intranasal structures or as a vehicle in displacement therapy, they occupy a highly important position in the rhinologist's office.

If nose drops must be prescribed for home use, only those which meet certain requirements should be considered. They should as nearly as possible simulate the normal secretions of the nose. They should be isotonic and non-detrimental to ciliary activity; they should also be non-irritating with a pH slightly on the acid side, and they should not be of the type which leads to a dependency on their use. Ephedrine 0.5 per cent in normal saline solution and many of the synthetic sympathomimetic preparations now available fulfill the requirements.

Instillation in a head-low posture is perhaps the most effective method of applying intranasal medication. The patient is placed on his back on a treatment table or bed, with his head extended so that it hangs over the edge of the table. The Proetz position calls for an extension sufficient to place the chin and the ear in the same vertical plane. In the Parkinson side-posture position, the patient is on the side with his head hanging over the edge.

The latter position is used with older people, those with thick necks, and those who complain of a feeling of flightiness or dizziness when the head is hyperextended.

Displacement Therapy

During the forty years since its origin,

the Proetz technic of introducing fluids into the sinuses has gained considerable vogue both in this country and abroad. This method is not advocated for use in the treatment of an acute cold or in the presence of an elevated temperature. It is, however, regarded as our one effective non-surgical means of dealing with chronic ethmoiditis or low-grade long-standing nasal infections.

Technic

The patient is placed on a table in the Proetz position while decongestants are instilled into the nose. After 30 to 60 seconds the nasal cavities are filled with warm, normal saline solution. Displacement is produced by alternative suction with release of suction a few times. If mucopus is withdrawn or blown out later, a positive diagnosis of ethmoiditis may be made.

Summary

Throughout the years, medicaments have been packed, sprayed and instilled into the nasal cavities by physicians in their treatment of various ailments of the nose and sinuses. It is, however, a known fact that little is to be gained by use of most of the methods of intranasal medication so far devised. Unfortunately, during the early decades of rhinology, little was known of the function of the intranasal structures that were being treated, and it was not until the mid 20's that much interest was displayed by rhinologists in nasal physiology and histopathology.

Intranasal medication at the present time is dependent largely on decongestant nose drops, which are not a great improvement over the medications of the past.

The shrinking effect of ephedrine and many of the other synthetic sympathomimetic preparations on the swollen nasal membranes of an acute head cold affords immeasurable relief, yet excessive use is discouraged, for the benefits must be weighed against the detrimental effects of the application which removes protective hyperemia of the nasal tissues, lowers local resistance and violates the principles of acute inflammations. It would seem then that the ideal nose drop

has not yet been discovered and that its discovery will have to be delayed until we learn more about the conditions which cause swelling of the nasal mucosa. A great step was made in this direction when it was deter-

mined that most of the stuffy noses for which sub-mucous resection was carried out received no improvement in their blockage until their nasal allergy also was brought under control.

President's Letter
(Continued from page 807)

coming in from all over the state.

I would suggest that a private, separate facility be built close by the Medical School, housing the offices of a number of family physicians, also interested in teaching, who could be made part or preferably full-time faculty members, but who would use the various departments within the University Hospital for their referrals, wherever possible for and agreeable to their patient-clientele. In this way all students could spend part of their time working in this private-practice setup, seeing many of the routine cases that come into the average family physician's office, which they would never otherwise get exposed to on their way through school.

Thus, by both precept and exposure more students might decide that they would prefer this type of practice, and thus begin to resolve the shortage problem. Admittedly this would take time; but it might pay off in the long haul. Their patients would be almost entirely private patients; the so-called charity or welfare patient is going to become an ever-diminishing quantity with "Uncle" footing the bill in ever larger numbers.

Let these thoughts of mine hopefully add something constructive to the other ideas which will be generated over the next few years for solving the very vexing problems of medical care and teaching with which we are now critically faced.

I am delighted to have the opportunity to pay my own tribute, as well as that of the entire Minnesota State Medical Association membership, to a man who has been a tremendous teacher and friend of so many of us who have been graduated from the University of Minnesota. Dr. Larry Boies succeeded one department head whose shoes were very large indeed, Dr. Horace Newhart, nationally recognized as one of the top men in his field. Dr. Boies has completely measured up to Dr. Newhart's image, in the opinion of those who know him best, and this is the greatest accolade I can give him. This issue is devoted to Larry's specialty, ENT, and it could not happen to a finer man.



C. G. Sheppard, M.D.
President
Minnesota State Medical Association

Formula for a Soporific Sponge

Take of opium, juice of hyoscyamine, unripened berry of the blackberry, lettuce seed, juice of hemlock, mandrake, ivy . . . put these all together into a vessel and plunge therein a new sea sponge just as it comes from the sea, taking care that fresh water does not touch it. Then put this sponge in the sun during the dog days until all the liquid is evaporated. And when there is need, dip it a little in water not too warm, apply it to the nostrils of the patient and he will quickly go to sleep. When you want to awaken him, apply juice from the root of the fennel and he will soon bestir himself.

Nicholas of Salerno: Antidotarium (12th century)

Aural Symptoms of Psychosomatic Origin

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Syracuse, New York

THE EXACT SEQUENCE of physical changes which takes place as a result of a psychosomatic disturbance has been the subject of considerable debate. Vasospasm as a result of tension is the most frequently mentioned cause. However, fear, anxiety, frustration, guilt and sorrow appear to create the same physiological change.

Various parts of the body such as the brain, the heart, the stomach, the intestines, the skin, the eyes and the ears may be the shock organs which give rise to upsetting symptoms. While the stomach appears to be the organ most frequently involved, the ears are not far behind.

Psychosomatic Turmoils

There are four main symptoms pertaining to the ear which may be due to psychosomatic turmoils. These are itching of or in the ear, tinnitus, loss of hearing, and dizziness. There are other symptoms, of course, but these four occur with the greatest frequency. To state that the four are always psychosomatic in origin would be erroneous, for each in turn may also have an organic etiology. As a matter of fact the etiology of any of the symptoms mentioned may be both organic and psychosomatic. It is sometimes difficult to assay which is the more important component.

Itching

Itching of the ears will be discussed first because in reality it is not an ear symptom. It is only one location where skin reactions may be manifest. However, for the person involved it can be a very annoying symptom. The very best management is to leave the itch in isolation, not to scratch it. Few victims resist the temptation to do so. The usual result is an aggravation of the original symptoms and this often results in complications which can be more annoying than

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the original condition. Scratching often introduces infection and if infection is present scratching can be vigorous enough to cause an abrasion of the skin. When a break of the skin occurs in the presence of infection, very painful furuncles or abscesses of the ear canal can follow. The best management of itching of the ear, then, is to ignore it — which can be done with the use of sufficient will power. The physician consulted should remember that the itching is only a manifestation of a disturbance of the skin and he should direct his attention to putting this portion of the body in the best possible condition. He should give some thought to discovering a possible psychic cause. It is often present.

Tinnitus

Probably everyone throughout all history, at one time or another, has been the subject of the sensation of tinnitus. But with the vast majority this has been momentary and very infrequent. The cause of these only seconds-long experiences is debatable, but it is probably vascular in nature. Their significance is negligible. When tinnitus is constantly present (heard for hours on end) it is another matter. This form of tinnitus usually represents some deterioration of the nerve of hearing or of its central connections. The tinnitus can take many forms. It can be a ringing, a roaring, a buzzing, a whistling, and be high pitched or low pitched. It can be steady or pulsating. If it is pulsating in character its cause is most likely to be a gross vascular lesion, i.e., arteriosclerosis or an arteriovenous aneurysm. If so, it is organic in origin and is not a matter of concern for this paper. The origin of tinnitus can be strictly organic, caused by any agent which would bring about a loss of function of the nerve of hearing. Human beings are exposed to many such agents. Life is full of such expectancies. It is surprising that *all* adults do not have tinnitus. If physical causative factors are so abundant, what part does the psyche play in the origin of tinnitus?

It is possible that the cause of tinnitus can be entirely psychogenic. The ears and

the eyes are the most sensitive organs of the body. Any disturbance of the vascular supply to the ears can result in temporary derangement of the function of the nerve of hearing. If the disturbance is temporary the resulting tinnitus may be fleeting in character. An occasional psychogenic disturbance thus may result in little or no tinnitus. A prolonged or a severe emotional experience may be the cause of a lengthy or even a permanent tinnitus. If the ear happens to be the individual's most sensitive shock organ tinnitus is more apt to ensue.

Tinnitus can be tolerated. This is the most important message a physician can give to his patient. Almost every victim of tinnitus has had the thought that his tinnitus is a symptom of a brain tumor. When the character and import of this symptom is explained, the patient is vastly relieved. Tinnitus is always worse when the patient is tired or nervous. Thus it can be a signal to which attention should be paid so that rest should be taken or a change in thinking should be made.

The sensation of tinnitus is controllable. The author has a constant tinnitus, yet for better than 99% of his waking hours he never "hears" it. At the moment of this writing it is ringing full blast. His attention has been called to it. The psyche then can be used to "cure" tinnitus. Here the psyche can play one of its most important roles in aural symptoms of psychosomatic origin.

Hearing Loss

Most hearing losses are caused by organic etiologies. But the same mechanism which is at work in creating tinnitus can cause a hearing loss. Perfectionists and "worry warts" are more susceptible than calm, care-free individuals. It is not often that a severe bilateral hearing loss can be attributed to psychosomatic causes, but occasionally this is true. However, a severe bilateral loss can occur, particularly if the individual is a highly susceptible person, as shown by lesions (from the same cause) in his heart and stomach or in other shock organs. If a patient has had a stomach ulcer for years and has had one or two coronary episodes,

and if a hearing loss exists, it is likely that the loss is psychogenic. Fortunately many of the hearing losses which can be attributed to psychogenesis are moderate in degree. Occasionally there is a severe unilateral loss which may be due to emotional disturbances.

The psyche plays another role in hearing losses. This is when there is a psychogenic loss as an overlay on a true organic loss. Mostly this is found in patients who subconsciously wish to "use" their hearing loss to their own advantage. The hearing loss is not as great as it is pretended (consciously or unconsciously) to be. To separate one from the other and prove that in reality the overlay does exist takes a large measure of diagnostic skill.

Finally, there is the psychogenic loss which is present when a patient has normal hearing. In large measure this is created when an escape from reality is desired or when it is "needed" as an attention getter. The attention-getting motive is more often found in children, the escape motive in adults, though the motive for the "loss" may be just the opposite. Most adults have the "loss" because they do not want to hear. Children have it to get the love and attention which they crave and are not getting. The cure for such losses is psychological or psychiatric.

Dizziness

Dizziness arises from involvement of the ear in a different location than when hearing is altered. It arises from disturbances in the labyrinth rather than in the cochlea to which attention has been drawn to this moment. Dizziness is a sensation of motion when there is none. The complaint of dizziness is common and may vary from a slight sensation of imbalance to a whirling sensation which is so severe that the patient may hold on to the head of his bed because he does not wish to fall off.

There are two problems connected with dizziness to which a physician should be alert. The first is to determine if possible that dizziness truly exists. Light-headedness is not dizziness, yet it may be difficult to ascertain which one of the two is present. **The differentiation must be made chiefly by**

careful history taking. There are few occasions in medicine that cry out for more careful probing. Some patients cannot describe their sensations accurately. This puts a double onus on their doctor.

The second problem is to determine, if possible, whether the dizziness is due to a peripheral origin (the ear) or a central origin (the central nervous system). The solution of this problem lies more in the realm of the physical examination than in history taking.

Psychic factors which cause dizziness more often affect the ear than the central nervous system. If a hearing loss in one or both ears is a concomitant symptom, it is probable (though not certain) that the organ giving rise to the dizziness is the ear.

There are several organic causes for involvement of the labyrinth. But psychic factors can and do affect this organ. They must, however, affect one labyrinth more than the other, for the two labyrinths must be out of balance if dizziness of the aural origin is present. Psychic factors do just that, affect one ear more than the other. It is a well known anatomical fact that no two sides of the body are exactly alike, and this is probably the reason why so often one ear is involved and not the other.

What we are saying is that vascular changes brought about by psychosomatic disturbances affect the labyrinth as well as the cochlea. Vascular changes are present at the time of the menopause. Add to this the psychic storms which menopause creates and you have good reason for the prevalence of dizziness in women at that time.

In the opinion of this author there are many more instances of dizziness due to psychic factors than there are due to organic causes. Seventy-five percent of labyrinthine tests performed on patients whose history or other physical examination suggests the necessity for caloric testing have a response to the test that is within normal limits. When both normal responses and dizziness are present in the same patient it may be assumed that there is no organic pathology in the labyrinth and that the dizziness is the result of abnormal physiology.

Altered physiology is the first stage in the course of psychic disturbances. Later irreversible pathology may come into the picture. This often happens. The time to nip dizziness in the bud, if it is psychogenic, is at its outset.

Conclusions

Story after story could be told of psycho-

somatic origins of aural symptoms. But this would unduly lengthen this presentation. Suffice it to say that they do exist and they can be the most exciting detective stories. The trouble is that too many doctors think they are too busy to solve these puzzles with which they are confronted.

Test Your Word Score

Enmeshed — *entangled* (page 820).

Polytomography — *sectional x-rays* (page 830).

Microtia — *small auricle or pinna of ear* (page 842).

Gustation — *tasting* (page 845).

Epistaxis — *epi, on + stazo, to fall in drops* (page 849).

Hypoproteinemia — *low protein content in blood plasma* (page 860).

Presbycusis — *inability to discriminate sounds* (page 870).

Achalasia — *failure to relax* (page 924).

Synkinesis — *an associated unintentional movement accompanying a voluntary movement* (page 986).

Adage — *a saying which has obtained credit by long use* (page 989).

If a man look sharply and attentively, he shall see fortune; for though she be blind, yet she is not invisible. — Bacon

The solar system has no anxiety about its reputation. — Emerson

Allergic Dysfunction

The Fundamentals

HARRY P. SCHENCK, M.D.*
Philadelphia, Pennsylvania

TO SOME EXTENT, recent investigations have clarified the role of the eosinophile in allergy by providing new information concerning other cells participating in tissue changes due to allergy.

Although Paul Ehrlich discovered basophilic tissue granulocytes in 1877, giving them the name of "mast cells" and reporting their increased number in chronic inflammation of connective tissue as well as the reciprocal relationship of mast cells and eosinophiles, 80 years elapsed before the recognition of the collagen diseases again focused the attention of investigators on the physiological and pathological significance of these biologically active cells.

Location of Allergic Pathology

The pathology in various allergic diseases, including hay fever, perennial nasal allergy and vasomotor rhinitis, is primarily in the ground substance of the connective tissue and consists of edema accompanied by an increase and liquefaction of the amorphous substance. Of the main cellular constituents of fibrous tissue, fibroblasts are concerned with the production of collagen fibers, whereas mast cells produce hyaluronic acid which has a regulating influence on ground substance, and also store histamine, heparin and many other substances which they liberate in the inflammatory chain reaction.

The Role of Mast Cells

Mast cells participate in the earliest phase of the local reaction of connective tissue to injury. They are the source of numerous substances, of which the most important are heparin, histamine and 5-hydroxytryptamine, and contain large granules which are dispersed extra-cellularly when they rupture or degranulate under the influence of many exogenous and endogenous substances. Various histamine liberators induce swelling, vacuolation and, finally, disruption of the mast

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cells with liberation of their contained granules. There is then an immediate release of histamine which produces vasodilation of the regional vessels, flooding of the injured zone with protein-rich lymph, and by direct action on the nearby connective tissue cells, increases their phagocytic activity and capacity. The connective tissue cells promptly ingest and digest the heparin-containing mast cell granules and are stimulated to produce mucopolysaccharide ground substance of their own.

Antigen-Antibody Reaction

It is probable that the antigen-antibody reaction underlying allergic reactions depends upon the exposure of plasma cells to the antigen followed by the manufacture and release of specific antibodies by the exposed cells. The specific antibodies, when released from plasma cells, become attached to accessible mast cells. When the specific antibodies produced by plasma cells reach such altered mast cells, a reaction takes place between the antigen and the antibodies attached to the mast cells, resulting in lysis of the mast cells and distribution of the granules of heparin or a heparin-like substance in the extracellular spaces.

The Plasma Cells

The role of the plasma cell in antibody formation is limited to the synthesis of gamma globulin which contains practically all of the humoral antibodies. While most antibodies are produced within lymph tissue where the cellular response is predominantly lymphocytic, lymphocytes do not manufacture antibodies although they play an important role by providing the energy and raw materials essential for the synthesis of antibodies by plasma cells during the course of lymphocyte degradation. The function of reticuloendothelial cells and leukocytes is probably limited to the splitting of aggregated or corpuscular antigen into chemically active antigenic molecules capable of stimulating the synthesis of antibodies by plasma cells.

The Circulating Cells

Mast cell lytic antibodies are not neces-

sarily specific to these bodies and they are also very active in causing damage to other cells. In localized allergic lesions, observed at an early stage, there is arteriolar contraction with obliteration of the lumina of the arterioles and temporary stoppage of the circulation due to action on the smooth muscles of the vessels. There is also an increased adherence of leukocytes to the blood vasculature endothelium, and emigration of leukocytes in large numbers through the walls of the capillaries and venules. The leukocytes within the capillaries stick to each other to form clumps, or emboli, which block the circulation in many of the capillaries and venules; but these manifestations are reversible and cease when the specific antibody is no longer available.

Normally in the upper respiratory tract, eosinophiles are distributed in the main in the middle submucosal layer and directly bordering on the epithelium and very rarely in the deep submucosal layer; mast cells are present almost exclusively in the deep submucosal layer. During active nasal allergy, degranulation of mast cells and release of histamine appear at an early stage and, if the reaction continues, there is a drastic numerical decrease which may continue until no identifiable cells of this type can be found even in the deep submucosal layer of the epithelium. Concomitantly with the mast cell decrease is an increase in eosinophiles which tend to occupy the entire submucosa. It is believed that the eosinophiles are attracted by the histamine present and proceed to alter or destroy it. Wherever edema is most marked, few or no mast cells are found, but eosinophiles are numerous. When the antigen-antibody reaction subsides, mast cells reappear and the number of eosinophiles diminishes.

Mast cells are sparse or absent in mucous nasal polyps although a few may remain in the deeper tissue near the attachment of the polyp. On the other hand, eosinophiles may be numerous at certain stages and are mostly concentrated in areas containing a greater histamine concentration. Plasma cells appear in large numbers in polyps containing polyp fluid with a high gamma globulin con-

tent but there is no correlation between the number of eosinophiles present and the increase of gamma globulins in the polyp fluid. Here, as elsewhere, wherever an appreciable quantity of histamine can be demonstrated, no undamaged mast cells are found as a result of their degranulation with the liberation of histamine.

Conclusions

A direct approach to the solution of the role of the eosinophile in allergy has been frustrating in the past, but the enigma appears to be much nearer solution with the recent dynamic extension of our knowledge concerning all of the cellular elements involved in allergy and anaphylaxis.

Gerlier's Syndrome

This syndrome is characterized by paroxysmal attacks of severe vertigo and muscular weakness. It was described by Felix Gerlier of Switzerland in 1887. Because this unusual condition occurs in limited areas geographically, little is known concerning it except the symptomatology. Sudden severe vertigo is usually the first symptom. Drooping of the eyelids partially obscures vision. There is pain in the nuchal and spinal muscles, followed by weakness of the cervical muscles with inability to hold the head erect. Severe vertigo and weakness of the limb and trunk muscles may make sitting or standing impossible. Attacks are episodic and may recur daily or more frequently, with varying degrees of severity in different persons.

Most of the reported cases of the syndrome have occurred in southern Switzerland and in Northern Japan almost invariably during the summer months. It most commonly occurs in healthy young farm workers, often in several members of a family. The etiology remains obscure. The degree of incapacitation may be mild or severe and prolonged for a few months. Treatment is symptomatic. In most cases complete recovery ensues after the onset of cold weather.

Durham, Robert H. — *Encyclopedia of Medical Syndromes*
Hoeber Medical Division, Harper and Row, New York

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Cervical Lymphography

The Present Status

MELVIN E. SIGEL, M.D.*
Minneapolis, Minnesota

LYMPHOGRAPHY, A METHOD for study of the lymphatic system using radiopaque contrast agents, received its prime impetus in 1952 when Kinmonth described a method for lymph-vessel cannulization allowing insertion of contrast agents directly into the lymphatic system. The primary usefulness of this technique was in delineating lymphatic pathways of the upper and lower extremities as well as the retroperitoneal area.

In 1960 (Battezzati, Pietrantonì), techniques were developed for cannulization of the cervical lymphatic system allowing visualization of the cervical lymphatics and lymph nodes with water-soluble contrast agents. Further modifications and revisions in this technique, particularly the better-quality radiographs produced by oily contrast agents, demonstrated greater predictability in the study of the cervical lymphatic network (Jackson 1963).

Cervical Lymphatic Pathways

The excitement engendered by radiographic demonstration of the cervical lymphatics was understandable. Perhaps this method of study would supply acceptable answers to poorly-understood patterns of cervical lymph-node patterns. Also, pathways in the neck as well as cervical lymphatic routes sought by metastasizing carcinoma of the larynx, oral cavity, sinuses and other head and neck regions might be more readily studied. Alterations in lymphatic flow secondary to cervical malignancies, surgery on the head and neck and lymphatic changes brought about by x-ray therapy to the neck could perhaps be studied and evaluated with this direct and reproducible technique.

Technique

The technique, as modified by Fisch and

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Bibliography available on request (801 Physicians and Surgeons Building, Minneapolis, Minnesota).



Fig. 1-a — Cervical lymphogram with good lymphographic-demonstration of the cervical nodes.

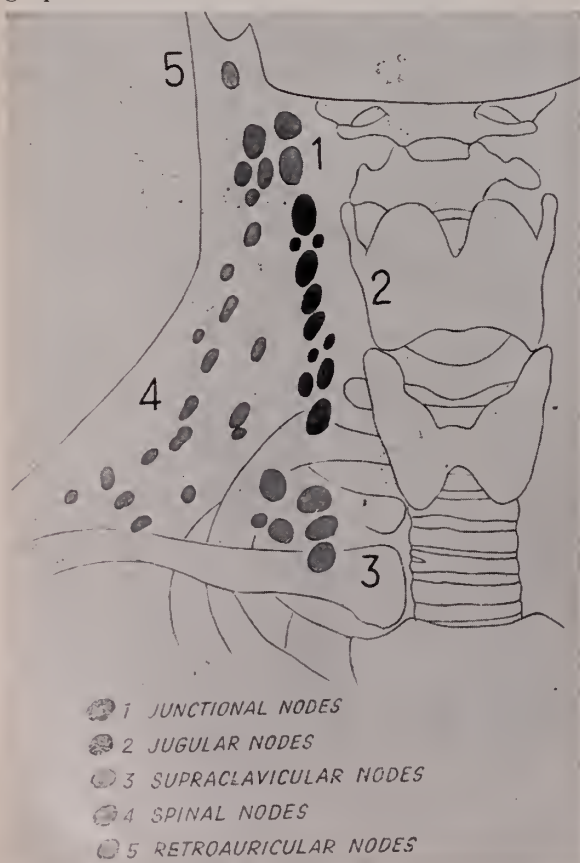


Fig. 1-b — Schematic representation of lymph nodes demonstrated by this method.

del Buono (1963) and further refined by Fisch and Sigel (1964), consists in administration of the oily contrast fluid, Lipiodol ultra-fluid, into a deep post-auricular lymphatic vessel using magnification afforded by the otomicroscope, following which, x-rays of the injected site are taken.

Observations

To date, certain observations may be attributed to this procedure of direct lymphatic cannulization and injection of contrast agents into the cervical lymphatic stream.

A demonstration of the normal lymphatic-flow pattern and lymph-node network comprising the deep lateral cervical lymphatic system with a functional classification of these lymph nodes by their lymphographic-filling characteristics into junctional, jugular, supraclavicular, spinal and retroauricular nodes has been possible (Figures 1-a and 1-b). Demonstration of the junctional group acting as a functional unit through which the spinal and jugular chains appear to fill has been of particular interest (Fisch and Sigel, 1964).

Changes in lymphatic flow-patterns brought about by surgical extirpation of cervical lymphatic tissue, such as in radical neck dissection, have been studied, demonstrating lymphographically a block to lymphatic flow at the resected sites with the lymphatic channels seeking alternate (including contralateral) drainage pathways (Sigel and Fisch, 1965).

Changes in the lymphatic system brought about by x-ray therapy to the neck have been evaluated, demonstrating continued though diminished flow through these radiated lymphatics and lymph nodes.

The most hoped-for clinical use of cervical lymphography, that is, the detection of non-palpable lymphatic metastases by lymphangiographic methods, has been partially stymied by the observation that non-specific lymph-node reactions, such as lymphoid and reticular hyperplasia, may give lymphographically-similar radiographs to those seen with metastatic disease (Fisch, 1964).

Conclusions

At the present time, cervical lymphography is still most readily applicable in an experimental setting due at least in part to the difficulty of the technique. However, any system of study which so clearly demonstrates the lymphatic system as does lym-

phangiography must be considered to hold great promise; and further refinements in technique as well as new contrast agents may eventually yield in cervical lymphography a valuable tool for the study of metastatic pathways in malignant disease of the head and neck.

King Charles II at the Mercy of His Doctors

Some idea of the nature and number of the drug substances used in the medicine of the past may be obtained from the records of the treatment given King Charles II at the time of his death. At eight o'clock on Monday morning of February 2, 1685, King Charles was being shaved in his bedroom. With a sudden cry he fell backward and had a violent convulsion. He became unconscious, rallied once or twice, and after a few days died. Seventeenth-century autopsy records are far from complete, but one could hazard a guess that the king suffered an embolism or else his kidneys were diseased. As the first step in treatment the king was bled to the extent of a pint from a vein in his right arm. Next his shoulder was cut into and the incised area "cupped" to suck out an additional eight ounces of blood. After this homicidal onslaught the drugging began. An emetic and purgative were administered, and soon after a second purgative. This was followed by an enema containing antimony, sacred bitters, rock salt, mallow leaves, violets, beet root, camomile flowers, fennel seed, linseed, cinnamon, cardamon seed, saffron, cochineal, and aloes. The enema was repeated in two hours and a purgative given. The king's head was shaved and a blister raised on his scalp. A sneezing powder of hellebore root was administered, and also a powder of cowslip flowers "to strengthen his brain." The cathartics were repeated at frequent intervals and interspersed with a soothing drink composed of barley water, licorice and sweet almond. Likewise white wine, absinthe and anise were given, as also were extracts of thistle leaves, mint, rue, and angelica. For external treatment a plaster of Burgundy pitch and pigeon dung was applied to the king's feet. The bleeding and purging continued, and to the medicaments were added melon seeds, manna, slippery elm, black cherry water, an extract of flowers of lime, lily-of-the-valley, peony, lavender, and dissolved pearls. Later came gentian root, nutmeg, quinine, and cloves. The king's condition did not improve, indeed it grew worse, and in the emergency forty drops of extract of human skull were administered to allay convulsions. A rallying dose of Raleigh's antidote was forced down the king's throat; this antidote contained an enormous number of herbs and animal extracts. Finally bezoar stone was given. Then says Scarburgh: 'Alas! after an ill-fated night his serene majesty's strength seemed exhausted to such a degree that the whole assembly of physicians lost all hope and became despondent: still so as not to appear to fail in doing their duty in any detail, they brought into play the most active cordial. As a sort of grand summary to this pharmaceutical debauch a mixture of Raleigh's antidote, pearl julep, and ammonia was forced down the throat of the dying king.'

King Charles was helpless before the drugging of his physicians, who wished to leave no stones unturned in his treatment.*

*Haggard, Howard W.: *Devils, Drugs, and Doctors*. Blue Ribbon Books, Inc., New York City, 1929, p. 334.

Minnesota Medicine at a Glance

Research in Otology — Lawrence

Page 813

From the first awareness that aerial vibrations were involved in the production and transfer of sound 400 years ago to the development of modern surgical techniques for the correction of deafness due to otosclerosis, the sequence of experimental study presents a long and interesting history. To otologists the field is still wide open for further advancement.

Otosclerosis — House

Page 817

Within the past ten or twelve years surgery for hearing loss due to otosclerosis has proven to be satisfactory in a high percentage of cases. The physical technique is not beyond the ability of one who has been adequately trained; therefore this procedure offers an opportunity for many individuals to receive improved hearing function.

Management of Acoustic Tumors — House and Hitselberger

Page 873

Surgical techniques used to remove acoustic tumors have been developed and a system of operations is now available to remove these tumors at every stage of their development without a disproportionate increase in surgical mortality.

Adenotonsillectomy — Donaldson

Page 933

Too frequently adenotonsillectomy has been used without adequate indication. Reasonably well controlled studies indicate that adenotomy rather than adenotonsillectomy is indicated for recurrent acute otitis media and recurrent middle ear fluid. The indications for tonsillectomy vary with age.

Bell's Palsy — Shambaugh

Page 985

Though Bell originally recognized the effect of trauma in causing paralysis of the seventh nerve, most of the instances of Bell's palsy have been considered to be idiopathic, despite the fact that 70% of the cases revealed a history of abnormal cooling of the mastoid region. The rigid confines of the facial nerve within the fallopian canal makes it possible for compression to result from edema, with blocking of the electrical conductivity and the nerve impulses. With electrical stimulation it is possible to determine a normal excitability of the nerve or a progressive reduction in the nerve excitability, which would then signalize the need for operative reduction of the area of compression.

Episodic Vertigo — Williams

Page 1008

Episodic vertigo presents an annoying diagnostic problem often enough to give the clinician episodes of causalgia. In order to understand the problem more thoroughly, Williams has enumerated many, described some of the causative factors, and suggested varieties of treatment which have been used to ameliorate these symptoms. He points out that if it proves impossible to differentiate between the more probable etiologic factors by history and functional tests, a series of treatments, each based on a different working hypothesis, should be tried in order to find out from the therapeutic results which of such working hypotheses is the more correct. With this plan of attack, it should nearly always be possible to provide symptomatic relief to a number of disorders whose only connecting links are principally the symptoms of vertigo, dizziness or both.

Psychosomatic Turmoil in the Ear — Hoople

Page 1025

Though the stomach may be the major target for psychosomatic symptoms, the ear falls not far behind. Most of the subjective psychosomatic symptoms are manifest as itching, tinnitus, impaired hearing, and dizziness. The physician should take time to solve the psychosomatic puzzles.

Darwin to Lyell

Our ancestor was an animal which breathed water, had a swim bladder, a great swimming tail, an imperfect skull, and undoubtedly was an hermaphrodite! Here is a pleasant genealogy for mankind. . . . I take a jealous pride in my Simian ancestry. I like to think that I was once a magnificent hairy fellow living in the trees, and that my frame has come down through geological time via sea jelly and worms and Amphioxus, Fish, Dinosaurs, and Apes. Who would exchange these for the pallid couple in the Garden of Eden?

— Charles Darwin

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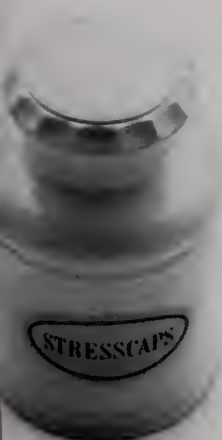
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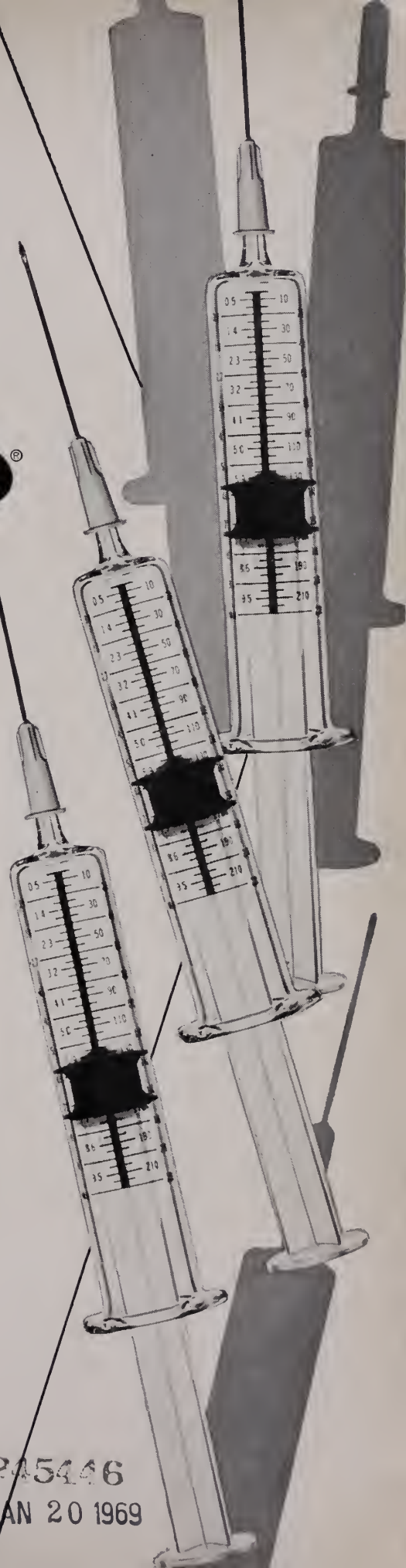
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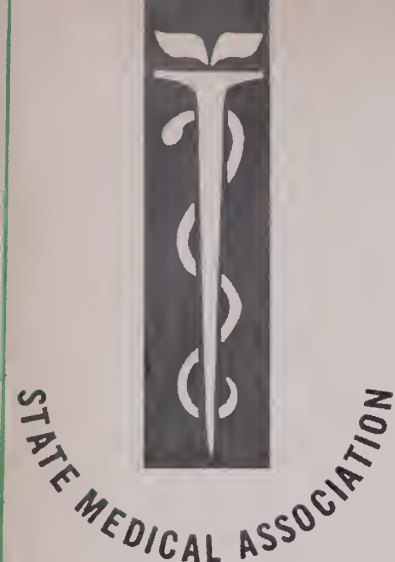
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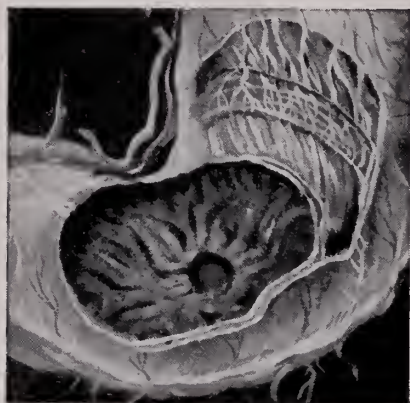
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References: 1. Batterman, R. C., and Grossman, A. J.: *Fed. Proc.* 14:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: *The Pharmacological Basis of Therapeutics*, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Roth, J. L. A., *et al.*: *Gastroenterology* 44:146, 1963. 4. Conney, A. H., and Burns, J. J.: *J. Pharmacol. Exp. Ther.* 128:340, 1960. 5. Settel, E.: *Clin. Med.* 6:1373, 1959. 6. Berman, H. H., *et al.*: *Dis. Nerv. Syst.* 25:430, 1964. 7. Darienzo, C.: *Ibid.*, 27:189, 1966.

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President's Letter

TRIBUTE SHOULD be paid to a dedicated group of people doing a fantastic job for the medical profession and the general public here in Minnesota. Their efforts are unique. I would recall your attention to a special article which appeared in the June, 1966, issue of MINNESOTA MEDICINE having to do with the work of the Pre-School Medical Survey of Vision and Hearing. Acknowledgement was made in that article of the tremendous work which a very gracious lady by the name of Mrs. John R. Stoltze has done in stimulating this rapidly developing program.

Dr. R. Hugh Monahan and his Committee on Ophthalmology sparked the whole effort and, with representatives of the Committee on Conservation of Hearing, the Survey was incorporated in 1959. Mrs. Stoltze was named executive secretary. The entire program is sponsored by the MINNESOTA STATE MEDICAL ASSOCIATION and administered by a Board of Directors composed of members of these Committees. The Survey is incorporated so as to receive gifts and gets its support from three sources: donated funds (which are deductible), the MS-MA, and temporary support from a Federal grant.

After 1959, when the program was started, it took two years for a group of audiologists under the direction of Dr. K. M. Simonton to develop a screening device called the Verbal Auditory Screen for Children (VASC). In 1961, the first full year of testing, only 1546 children could be tested, because of a lack of screeners as well as equipment. In 1966, by contrast, it had become possible to test 14,515 children.

The task ahead is enormous, but the way these people work makes a tremendously interesting story. Their goal is to be able eventually to test

all of the four-year-olds in the state, which number between 70,000 and 75,000 children. At the present time there are 35 "demonstrators." These are specially trained women, volunteers, usually housewives, including physicians' wives, Mrs. Jaycees, and other community-minded women, who do the job of training the screeners.

Over the state there are now about 4,500 screeners, and their numbers are growing rapidly each year, who will eventually be able to do the job they have set for themselves. They hope to double the number of children tested in 1967 over the 14,515 figure of last year. Eighty percent of the medical reports received have been positive, a remarkable testimonial to the equipment which has been devised, and certainly to the efforts of all those involved in the program.

This entire task has of necessity grown slowly at first, but now it seems to be snowballing to the point where their goal will be reached within a very few years. These service clubs, who have been sponsoring this effort, the Woman's Auxiliary to the Minnesota State Medical Association, the PTA's, the Mrs. Jaycees, Jaycees, Lions, Kiwanis, Rotary, hospital auxiliaries, and many others should be given our great vote of thanks for the work they are doing for our children.

Whenever the program is started in a community, the physicians should be wholeheartedly behind it, for without these trained lay people doing the job, it could never be done.

C. G. Sheppard, M.D.
President

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Cystic Fibrosis

Nature

and

Prognosis*

WARREN J. WARWICK, M.D.**

Minneapolis, Minnesota

ALTHOUGH CYSTIC fibrosis is a fatal disease, it may be compatible with a normal life if adequate treatment is started early. We can resolve this paradox by considering the relationship of the inherited metabolic defect to the complications which form the syndrome recognized by clinicians as cystic fibrosis.

Clinical Manifestation

The clinician sees cystic fibrosis as a chronic pulmonary disease with pancreatic insufficiency and an increased amount of salt in the sweat. He suspects the diagnosis in infants and young children who gain weight poorly, have steatorrhea, develop rectal prolapse, acquire a persistent cough, pulmonary atelectasis or multiple pulmonary infections. He confirms his suspicion on the basis of a sweat chloride or sodium in excess of 60 meq/L. His clinical experience has taught him that death is likely to occur in a few years even if he uses many antibiotics for treatment and prophylaxis of infections as well as pancreatic enzymes to control the bowel symptoms and a high vitamin and protein diet to prevent deficiencies.

Abnormal Exocrine Glands

How then may a normal life be possible? To understand this contradiction we must arbitrarily distinguish the inherited metabolic defect from the clinical syndrome. The inherited defect is transmitted by a single gene on an autosomal chromosome and is present in every fetus who receives such a gene from both parents. The direct consequences of the inherited genetic defect is the formation of abnormal exocrine glands and the elaboration of abnormal secretions. The clinical syndrome is the result of complications

*USPHS Research Career Development Awardee K3-A5, 14,035

This research was supported by a Cystic Fibrosis Care, Research and Teaching Center grant from the National Cystic Fibrosis Research Foundation and a grant-in-aid from the Minnesota Cystic Fibrosis Chapter.

**Associate Professor of Pediatrics University of Minnesota Medical School.

caused by the abnormal secretions. A normally active life may be possible if prophylactic therapy can be used to prevent or to delay the onset of the potential complications.

Effects of Salt Depletion

The sequence from the inherited defect to the clinical complications and the prophylactic treatment necessary to prevent the complications is seen most clearly in the pathophysiology of the sweat gland. The nature of the defect is unknown, but the secreted sweat is recognized to be abnormal by the increased content of sodium and chloride. Clinical symptoms of salt depletion may develop after severe or prolonged sweating or a restriction of salt intake. Prostration, shock, and death may result. Prophylactic treatment, consisting of an increased amount of salt in the diet, will prevent these complications.

Pulmonary Complications

The sequence from the primary defect in the mucous glands to the pulmonary complications is similar but more complex, the complications more frequent and serious and the prophylactic treatment less well established. The nature of the mucous gland defect is also unknown, although the secretions of the mucous glands and goblet cells are abnormally viscous.

Bronchial Obstruction

Ciliary activity, increased velocity of expired air and coughing, which move normal bronchial mucus freely, are relatively ineffective in moving bronchial mucus in patients with cystic fibrosis. Thus, mucus accumulates and causes the first complications: partial bronchial obstruction with over-distention of/or total bronchial obstruction with collapse of the distal lung.

Infection

The lung handicapped by accumulating mucus is susceptible to infection, since bacteria entering the lung are normally trapped in mucus and expelled. The stagnant mucus in patients with cystic fibrosis permits bacteria to grow and to cause local infection. Infection in turn causes leukocytic and serum exudation and formation of intrabronchial pus, thus increasing the quan-

tity and viscosity of the retained secretions. The inflammation induced by the infection causes hypertrophy of the mucus-secreting glands and cells and loss of ciliated cells. Untreated, the process is progressive, culminating in bronchial destruction, pulmonary insufficiency, cor pulmonale and death.

Mortality

Since the abnormal mucus in the bronchial tree causes 99 per cent of the morbidity and 95 per cent of the mortality in children with cystic fibrosis, the prognosis for survival can be estimated by sole consideration of the pulmonary complications if the mortality caused by meconium ileus is ignored. Three assumptions are pertinent for this consideration. First, the earlier the treatment is started after symptoms begin, the longer the severe complications can be delayed. Second, if treatment can be devised to delay the onset of complications, prognosis should be further improved. Third, if the abnormal secretions could be made normal or the glandular defect corrected, a normal life would be possible. The first and second assumptions are supported by life tables made for children with cystic fibrosis receiving different types of treatment.

Generation Life Table

The life table approach makes it possible to summarize mortality rates for specific populations at specific periods and to obtain measures of comparative longevity such as the median length of life after birth or the proportion of persons surviving to specific ages. There are two types of life tables: the generation or cohort life table and the current life table. The "generation life table" provides a "longitudinal" perspective in that it follows the mortality experience of a particular cohort, all persons born in the year 1900, for example, from the moment of birth through consecutive ages in successive calendar years. Based on age-specific mortality rates observed during consecutive calendar years, the generation life table reflects the mortality experience of a cohort from birth until no lives remain in the group.

Current Life Table

The better known "current life table" may, by

contrast, be characterized as cross-sectional. Unlike the generation life table, it does not represent the mortality of an active cohort. Rather, the current life table considers a hypothetical cohort and assumes that it is subject to the age-specific mortality rates observed for an actual population during a particular period. Thus, for example, a current life table for 1960 assumes a hypothetical cohort subject throughout its lifetime to the age-specific mortality rates prevailing for the actual population in 1960. The current life table may thus be characterized as rendering a "snapshot" of current mortality experience.¹

When the limiting data for the cohort populations has been defined, comparisons can be made. The Figure shows survival curves for several cohort populations of patients with cystic fibrosis which were prepared from life table data. Curve G shows the life table curve for the whole United States population based on age-specific mortality rates for 1960. Curve A demonstrates the early onset and the malignant nature of cystic fibrosis as recorded in three reports published in 1938.^{2,3,4} This curve includes five patients diagnosed at the University of Minnesota prior to 1938.* No treatments were used prior to 1939, which would have altered the natural history of the complications of cystic fibrosis in these patients. The significant points to note in this representation of the natural mortality of cystic fibrosis are: (1) the median age at death was eight months of age; (2) over 70 per cent of infants died before age one; but (3) an occasional child survived beyond 10 years of age.

Treatment

After 1939 when sulfanilamide and antibiotics became available, treatment could be directed at pulmonary infections.

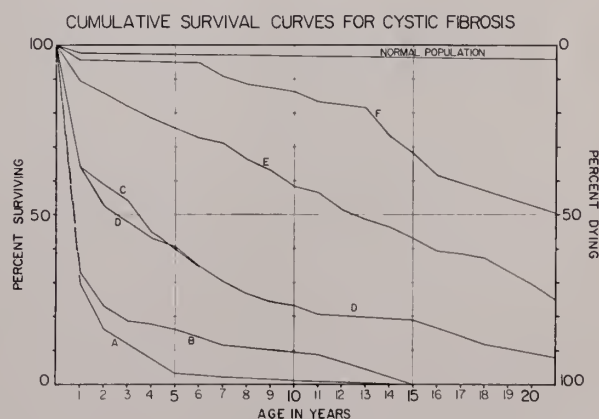
Antibiotic Medication

Two reports plus the records of the University of Minnesota Hospitals were complete enough to calculate life tables. The patients in these three studies received antibiotic treatment for pulmon-

ary infections and supportive measures including pancreatic enzyme replacement.^{5,6,7} Curves B, C and D show improved survival but great variation in the amount of improvement. If the two better curves are taken to be most representative of the improved prognosis for children with cystic fibrosis who received sulfa and antibiotic treatment, we observe that: (1) the median age at death increased to three years; (2) the proportion dying before age one decreased from over 70 to about 36 per cent; (3) survivors beyond age 10 increased from an occasional patient to nearly 10 per cent.

Pulmonary Hygiene

In the 1950's intensive pulmonary treatment, in particular aerosols by face mask and mist tent and physical therapy to the chest wall and lungs, began to be used to remove retained secretions from the lungs. These techniques form the basis for the present treatment of cystic fibrosis in Cystic Fibrosis Care, Research and Teaching Centers throughout the United States.⁸ Many variations are currently in use. In 1965, 31 of these Cystic Fibrosis Centers pooled data on the patients they followed and the deaths they observed in 1964.⁹ These data are shown in Curve E. In this cohort the improvement in survival is obvious: (1) the median age at death is shown to be 12 years; (2) the proportion dying before age one decreased to 11 per cent, and (3) survivors beyond age 20 increased to nearly 30 per cent.



Figure

*C.H. born November, 1933; died January, 1934—age 3 months
G.P. born October, 1934; died January, 1935—age 3 months
T.P. born July, 1937; died May, 1938—age 10 months
N.G. born August, 1937; died October, 1937—age 2 months
D.H. born October, 1937; died March, 1938—age 6 months

Results

The pulmonary therapy used at these 31 Centers was begun at varying times. Some Centers started pulmonary therapy prophylactically^{10,11} as soon as the diagnosis was made, with the advocated purpose of preventing or delaying the onset of the obstructive and infectious pulmonary complications. If prophylactic pulmonary therapy is of value, the survival curve for patients given this therapy should be better than the average pulmonary which is usually delayed until the obstructive and infectious pulmonary complications have begun. In the Figure, Curve F shows the survival curve for all patients with cystic fibrosis cared for at Babies and Children's Hospital, Western Reserve University, since the Cleveland Cystic Fibrosis Center was organized.¹² All patients seen between 1958 and 1966 including those diagnosed at autopsy are included. Patients seen once for consultation were excluded in order not to give a falsely good curve. The improvement in survival for this cohort appears to be significant: (1) the median age at death is estimated to be 21 years; (2) the proportion dying before age one is 4.3 per cent as compared to 2.3 per cent for the whole U.S. infant population in 1960; and (3) survivors beyond age 20 increased to over 50 percent.

In this group 24 deaths occurred in the 349 children under care for a total of 1,188 patient years. The children were followed for an average of three years five months. None were followed for more than eight years. The mortality at any point along Curve F after age four reflects the mortality for children diagnosed on the average three and one-half years earlier. In the early years of the curve when few complications were present at diagnosis and maximal benefit from prophylactic therapy could be expected, death, the ultimate complication, was frequently prevented. In the last part of the curve when more and severer complications were present in patients admitted to the study and less benefit could be expected, death occurred as frequently as in the last years of Curve E for the averaged pulmonary therapy.

Although more data will have to be collected

to separate and compare the value of prophylactic versus symptom-directed pulmonary therapy, survival with the prophylactic approach appears to be improved. Data such as these require confirmation by other centers* and warrant carefully controlled studies of morbidity as well as of mortality. However, continued collection and tabulation of mortality data on patients with cystic fibrosis treated at Cystic Fibrosis Centers will permit annual computation and comparisons of survival, longitudinal studies of cohorts of patients born in one year and diagnosed at different ages, and eventually comparison of therapies.

Evaluation of therapies by the life table technique reviewed in this paper is subject to few criticisms other than overt falsification of data, for death is a criterion universally acceptable for failure of a treatment program. However objective death is as an absolute criterion, it is not sensitive to subtle differences in the values of therapy, and vast amounts of mortality data would have to be collected, perhaps over extended years, to pinpoint that type of difference. Such a use of the life table technique would be either insensitive to, or biased by, inability to keep therapy constant over long periods of time. Comparison of therapies by the life table mortality end-point is not to prove one therapy better than another but to identify aspects of therapy which need carefully designed and controlled studies and to supply the stimulus to evoke these studies. This comparison of averaged pulmonary therapies vs. prophylactic pulmonary therapy suggests that controlled studies are needed to evaluate the philosophy and the specific components of the prophylactic approach to the pulmonary disease in children with cystic fibrosis.

Conclusions

Controlled studies of morbidity in matched newborn infants with cystic fibrosis appear to be the best way to evaluate the prophylactic approach. This need is now stimulating studies which may one day produce a practicable newborn nursery sweat test for cystic fibrosis.¹³ The aims of research beyond such a study are to find ways to directly normalize the mucus as it is being formed or to modify the cells of the mucous glands so that they will produce normal mucus. When either is achieved, patients with cystic fibrosis who do not have pulmonary complications should be able to live lives freed from

*Annual crude mortality rates for patients with cystic fibrosis treated at the University of Minnesota were: 1958—23.5%; 1959—29.2%; 1960—20%; and 1961—15.4% before starting prophylactic pulmonary therapy. Since then the rates have been: 1962—16.2%; 1963—3.2%; 1964—2.8%; and 1965—2.2%.

their present increased predisposition to bronchial obstruction and infection; then the goal of

prophylactic therapy, a normal healthy life, may be achieved.

References

1. Life Tables, Vital Statistics of the United States, Volume II, Mortality, Part A, Section 2, 1960.
2. Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relationship to Celiac Disease. *Amer J Dis Child* 56:344, 1938.
3. Blackfan, K. D., and May, C. D.: Inspissation of Secretion, Dilation of the Ducts, and Acini, Atrophy and Fibrosis of the Pancreas in Infants. *J Pediatrics* 13:627, 1938.
4. Harper, M. H.: Congenital Steatorrhea due to Pancreatic Defect. *Arch Dis Child* 13:45, 1938.
5. Bodian, M.: Fibrocystic Disease of the Pancreas. William Heinemann, London 1957.
6. Andersen, D. H.: Therapy and Prognosis of Fibrocystic Disease of the Pancreas. *Pediatrics* 3:406, 1949.
7. Warwick, W. J., and Monson, S.: Life-table Studies of Mortality. Proceedings, The Fourth International Conference on Cystic Fibrosis, Grindelwald, Switzerland, September 22, 1966.
8. Guide to Diagnosis and Management of Cystic Fibrosis. New York, New York. National Cystic Fibrosis Research Foundation, 521 Fifth Avenue, March, 1963.

9-13 May be secured from the author or the reprints.

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On studying the development of human intelligence, it is found that it passes through three stages: the theological, the metaphysical, the scientific or positive. In the theological stage it seeks to account for the world by supernatural beings. In the metaphysical stage it seeks an explanation in abstract forces. In the scientific, or positive, it applies itself to the study of the relation of phenomena to each other. At present the theological, the metaphysical and the positive conflict, and cause intellectual confusion. — Auguste Comte

Faith

MAN is a whole being; he cannot be divided into parts; he is not a jig-saw puzzle; he is a one-piece person. The patient is physical; he is spiritual; he is mental; and he is social in his total health. It is widely recognized that a weakness in any one of the four factors of his health can militate toward ill health in any one or all three of the other factors. We recognize immediately that all illness is not organic. The parents of the retarded child in some cases are more ill than is the child. Moments of shock, fear, hysteria, and grief are moments of serious illness and these illnesses can affect the whole being.

The faith of the individual is a vital factor in total health. The patient must be treated and cared for within the scope of that faith, because it is faith that gives courage, strength, patience, assurance, and hope—all of which aid in the healing process. These are not commodities that can be purchased in a bottle at the drug store but are intangible factors underlying every individual's basic philosophy of life and hence his total health.

Too frequently our illnesses are not organic ones that can be mitigated or cured by drugs; nor are they diseased areas that can be removed by a surgeon's knife. Instead, our illness requires therapy deep within our heart and our life. Because of the stress and strain exerted by the pressures and demands of the world, either we have forgotten that faith plays a vital and important role in our total well-being or we have thoughtlessly forsaken that faith.

To what extent do we maintain the patient as a mere vegetable? The practice of euthanasia or mercy killing is not involved here; medicine as a profession is opposed to both. The physician and the clergyman need to have dialogue in this area: they need to discuss this issue carefully—with understanding, compassion, and mercy, so that the physician can be assisted in making his decision a scientific and at the same time a moral one.

A person has the right to die with the dignity inherent in death itself. I question the use of extreme measures to prolong a merely vegetating life. With mechanical means we can sustain the beating heart; but is this life in the true sense? To allow a body to waste away to nothing but skin and bone is to refuse the human being his prerogative of dignity in death.

Herein lies the paradox of modern medicine: the fact that we have facilities and techniques to prolong and save lives; but that these same procedures can also be used to prolong mere existence.

A young teenage lad was seriously injured, resulting in total paralysis from the waist down. A mother and a father who had hoped and planned for their son's future now saw all their dreams tragically shattered. The young man himself who had lived day by day, full of ambition, energy, enthusiasm, now finds all these sparks extinguished. A wheelchair is to be his home. Where, I ask, do we turn to give this man the incentive to live?

Here then is the sphere of interplay between physician, clergy and family—the challenge to make this young man see that life is more than a pair of legs—that despite physical handicap, life can still be a wonderful adventure. It takes more than a drug, more than a surgeon's knife, even more than the love and compassion of a family. It demands faith!

Rev. Dr. Paul B. McCleave*
Chicago, Illinois

*Director Department of Medicine and Religion, American Medical Association.

|| Amniocentesis

Effect
of
Contamination
of
Amniotic
Fluid
with either
Maternal
Blood
or
Meconium

WILLIAM N. SPELLACY, M.D.*
W. D. COHEN, Ph.D.*
R. A. DIAMOND, M.D.*
Minneapolis, Minnesota

ONE OF THE MORE recent advances in the management of the Rh negative sensitized pregnant subject has been the introduction of studies of the amniotic fluid pigments. Of all available tools to the clinician this seems to have the best prognostic value. The procedure of amniocentesis^{oo} is safe. One not infrequent problem, however, has been the contamination of the amniotic fluid with maternal blood during the procedure, or the so-called "bloody tap." Another common contaminating substance is meconium. The effect of these substances in subsequent amniotic fluid analysis has not been well studied. The present study was undertaken in order to determine the changes produced in amniotic fluid pigment determinations by the injection of maternal blood into the amniotic cavity or from the addition of meconium to amniotic fluid.

Procedure

The patient was enrolled in the prenatal clinic at the University of Minnesota Hospitals and volunteered for this study. She was a 19-year-old gravida whose expected date of confinement was January 29, 1966. The patient's medical history was complicated by the presence of a congenital heart lesion which had been diagnosed as Ebstein's anomaly. Her cardiac history will be presented elsewhere. She had a serum bilirubin of 0.1 mgm. % at one minute and 0.3 mgm. % total. Her blood type was O CcDEe with a negative indirect Coombs test.

On 11/17/65, at 29 weeks of gestation, an amniocentesis was performed. After a fluid sample was removed for study, 10 ml. of the patient's blood was removed from an antecubital vein and injected into the amniotic (fluid) cavity. The patient had no adverse reaction to this procedure. Repeat amniocenteses were then performed on 12/2/65 (31 weeks of gestation); 12/16/65 (33 weeks of gestation); 12/30/65 (35 weeks of gestation), and 1/25/66 (39 weeks of gestation). The fluid samples were protected from light and immediately centrifuged at 2000 r.p.m. for 30 minutes to remove red cells and larger particles of vernix caseosa, and the supernatant was then filtered through retentive filter paper. The filtrate was then removed and the optical density was measured on a Beckman spectrophotometer

*From the Department of Obstetrics and Gynecology, University of Minnesota Medical School, Minneapolis, Minnesota.

**See Test Your Word Score Page 1097.

model B (calibrated for wavelength and photometric accuracy) between 325 and 700 millimicrons wave length. A chemical analysis of the supernatant bilirubin content was also done by the method of MacKay and Watson'. The results of the spectrophotometric and chemical analysis of these fluid samples are listed in Table 1.

TABLE 1

Changes in the Amniotic Fluid Pigments Produced
by the Introduction of Maternal Blood into the Amniotic Sac

PIGMENT STUDIED mgm %	CONTROL				
Methemalbumin of 625 mμ	0.03	0.31	0.18	0.02	0.28
Oxyhemoglobin of 415 mμ	0.83	1.82	0.73	0.96	1.76
Liley Units of Excess OD of 450 mμ	0.050	0.000	0.028	0.011	0.015
Chemical Diazo Bilirubin	0.057	0.046	0.031	0.000	0.045
	29	31	33	35	39
	WEEKS OF GESTATION				

The patient began labor spontaneously on 1/28/66, and after a total labor of 14 hours and 25 minutes she delivered a 3100-gram normal male infant over a left mediolateral episiotomy with the aid of low forceps and using paracervical and pudendal block anesthesia. The cord blood studies showed a hemoglobin of 17.5 grams %, and a one-minute bilirubin of 0.2 mgm. % with a total bilirubin of 1.9 mgm. %. The baby blood type was O CcDee with a negative direct Coombs test. Both the mother and infant have done well post partum.

Discussion

The use of amniotic fluid pigments to predict the severity of erythroblastosis fetalis was pioneered by Bevis in 1953.² This procedure has been extensively studied now by Walker, Liley and others.³⁻⁵ Both the simplicity of the procedure of amniocentesis and the relatively accurate prognostic index of the spectrophotometric analysis of the amniotic fluid have determined the wide acceptability of this test. The two major drawbacks to this method are: (1) the maternal and fetal complications and (2) the occasional false-positive test results.

The false-positive fluid analysis can be disastrous if the studies predict a severely affected infant and if the obstetrician prematurely delivers a normal unsensitized infant. False-positive results have occurred.^{6,7} The explanation for the presence of these abnormal pigments is unknown.

The maternal and fetal complications of am-

niocentesis have been described by several authors and include failed taps, bowel perforation, amnioitis, fetal hemorrhage, abruptio placentae, premature labor, and hemoperitoneum.⁸⁻¹² Zippursky has also suggested that further sensitization of the mother occurs from the spillage of fetal red blood cells into the maternal circulation at the time of amniocentesis.¹⁰ The occurrence of these complications is rare, however.

A more frequently encountered problem is the "bloody tap," where maternal blood is spilled into the amniotic cavity during amniocentesis.

The present study was undertaken in order: (1) to better understand the changes in the spectrophotometric analysis of amniotic fluid after maternal blood is accidentally put into the amniotic cavity and (2) to try to find a cause of the false-positive amniotic fluid analysis.

The results of this experiment show that oxyhemoglobin (415 mμ) and the methemalbumin (625 mμ) concentrations rise abruptly after the blood contamination. The major indicators of fetal Rh disease, the excess optical density (O.D.) at 450 mμ (Liley units) and chemically determined bilirubin, are not affected by the "bloody tap." The fluid pigments return to a normal state in approximately four weeks. Liley has noted that the pigments from traumatic tap disappear by three weeks.⁸ These results show that the false-positive test results are apparently not due to maternal hemorrhage into the amniotic cavity.

With the use of intrauterine exchange transfusion as a treatment for affected infants these data demonstrate that one may contaminate the amniotic fluid with blood and still be able to use the results of amniotic fluid withdrawn at subsequent examinations as a prognostic index for the fetus.

In the search for the cause of false-positive results meconium was studied. Fresh meconium

TABLE 2

Changes Produced in the Amniotic Fluid
Pigments by the Addition of Meconium

	Pigments in mgm%			
	Methemalbumin 625 mμ	Oxyhemoglobin 415 mμ	Chemical Diazo Bilirubin	Liley Excess O.D. 450 mμ
Control Amniotic Fluid	0.003	0.065	0.061	0.045
Control Amniotic Fluid plus 0.1% Meconium	0.77	2.54	0.073	0.057

was obtained at a breech delivery and a 1% suspension of this was made in 0.9% saline. To one of two aliquots of a normal amniotic fluid sample was added a 0.1% concentration of meconium. Both fluids were then subjected to complete analysis as previously described. The results of this experiment are recorded on Table 2. Here also there is no significant alteration in the two prognostic indices for erythroblastosis (chemical bilirubin and Liley excess O.D. units). The meconium contamination of amniotic fluid does not cause a false-positive interpretation in the management of an Rh sensitized pregnancy.

Summary

Maternal blood was placed in the amniotic cavity at 29 weeks of gestation and amniocentesis was repeated on four subsequent occasions. The pigments resulting from this procedure are described. There is no increase in the principal pigments used as prognostic indices for erythroblastosis fetalis. Normal amniotic fluid was also studied with and without the addition of meconium. The pigment alterations produced by this are described. The significance of these findings is discussed.

References

1. MacKay, E. V., and Watson, D.: The Prognostic Value of Bilirubin Levels of Amniotic Fluid in Rhesus Iso-Immunized Pregnancies. *Med J Aust* 49:942, 1962.
2. Bevis, D. C. A.: The Composition of Liquor Amnii in Hemolytic Disease of the Newborn. *J Obstet Gynec Brit Emp* 60: 244, 1953.
3. Walker, A. H. C.: Liquor Amnii Studies in the Production of Hemolytic Disease of the Newborn. *Brit Med J* 2:376, 1957.
4. Liley, A. W.: Liquor Amnii Analysis in the Management of the Pregnancy Complicated by Rhesus Sensitization. *Amer J Obstet Gynec* 82:1359, 1961.
5. Goodlin, R. C., and Schwartz, S.: Coproporphyrin Content of Amniotic Fluid in Normal and Diseased Infants. *Amer J Obstet Gynec* 84:808, 1962.
6. Crosby, W. M., and Merrill, J. A.: Spectrophotometric Analysis of Amniotic Fluid. Direct Assessment of Fetal Status in the Isoimmunized Pregnancy. *Amer J Obstet Gynec* 92:53, 1965.
7. Cohen, W. D.: Unpublished data.
8. Liley, A. W.: Errors in the Assessment of Hemolytic Disease From Amniotic Fluid. *Amer J Obstet Gynec* 86:485, 1963.
9. Fairweather, D. V. I., and Walker, W.: Obstetrical Considerations in the Routine Use of Amniocentesis in Immunized Rh Negative Women. *Brit J Obstet Gynec* 71:48, 1964.
10. Zipursky, A. Z., Pollock, J., Chown, B., and Israel, L. G.: Transplacental Foetal Haemorrhage after Placental Injury during Delivery or Amniocentesis. *Lancet* 2:493, 1963.
- 11-12. may be secured from the author or the reprints.

Our Stone-Age Peers

Let us not regard paleolithic man with contempt. We are heirs to centuries of science, and as we think of modern man's absorption in war, of the grade of intelligence exhibited in political campaigns, of the various religious cults which sprang up within recent years, of the quality of periodicals with the largest circulation, of the seances of spiritualists in all countries, of the numerous individuals who earn a livelihood by reading palms and casting horoscopes, we realize that we have little reason to be boastful.

Shall we laugh because the medicine-man, in order to increase his dignity, smeared his body with red paint? Let us rather recall that in the civilized centuries the mark of the physician was a red cloak. Shall we mock his magic stick, the mere sight of which made his people feel better? Not as long as we remember the vogue of its successor, the gold-headed cane. Shall we condemn him because he sought to mystify his patients with wonder-tricks and words they could not understand? Let us reflect on more modern practitioners who give detailed instructions about taking a cathartic pill. In all ages, the invalid quite as much as the attendant, has insisted on a certain amount of hocus-pocus with the treatment.

Intellectually, we are but a stone's throw from the Stone Age; and emotionally, we are still living there.*

*Victor Robinson, *The Story of Medicine*, 1931.

Laughing Gas

Everything necessary to scientific anesthesia was available for some time before its "discovery," waiting for someone to stumble across it and put it to use. And that, literally, is just about how it happened, through staggering and stumbling.

Sir Humphrey Davy had suggested the anesthetic use of nitrous oxide after he had tried it on himself and found that it had an intoxicating effect, making him feel lightheaded and lighthearted.

People disregarded Davy's anesthetic suggestion but took up the inhalation of nitrous oxide as a popular fad. It soon became fashionable to have "laughing gas" parties where people breathed nitrous oxide, or ether, which had a similar effect. It was a very amusing pastime. People inhaled the gas, became pleasantly intoxicated, staggered and stumbled about, talked foolishly, laughed loudly and lost some of their inhibitions.

The popularity of ether and "laughing gas" parties jumped the Atlantic and soon young people, especially students, had taken up the rage in the more populous areas of the Eastern seaboard of America. The whole business was so fascinating, especially because of its so-called "scientific" overtones, that patent-medicine peddlars and other itinerant showmen posing as "professors of chemistry" gave lectures and demonstrations which attracted the thrill-seekers and gullible in the small towns and villages of the countryside.

One such traveling showman was a tall young man of 18 with an incompleted preparatory school education. Decking himself out in a frock coat and a high hat, he proclaimed himself as "Dr. Coult of New York, London and Calcutta" and set out in 1832 to demonstrate the scientific wonders of "laughing gas."

With a home-made apparatus which he pushed about in a hand cart, he first toured the towns of Massachusetts, setting up in the public squares on market day and, after making a speech and demonstrating on himself, he would invite spectators to inhale the gas. These spectacles so amused the audiences that Dr. Coult often collected as much as ten dollars when he passed the hat.

The young man, as it happened, was raising money in order to be able to patent and produce a revolver he had developed. His name was really Samuel Colt of Hartford, Conn.

A skilled showman, he became part owner of a penny museum in Cincinnati, where he put on a laughing gas show in order to help raise funds for Canadian patents on his Colt revolver. This time he decided to hire some Indians to inhale the gas, hoping that the novelty would attract a large crowd. He was right. The museum was jammed with people, many of whom came armed in the morbid expectation that the Indians would go on a scalping rampage.

What actually happened came as a shock to all. The Indians, probably having inhaled too much gas, promptly fell asleep. Colt, fearing the crowd would think itself cheated of its thrills and start a riot, quickly called a local blacksmith to the stage and gave him a whiff of gas. The befuddled smith then began to chase Colt around the stage, knocking over the Indians and waking them in the process. This saved the show.*

*Bernard Seeman: *Man Against Pain*.

Nodular Disorders of the Legs

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NODULAR INFLAMMATORY lesions of the legs frequently pose diagnostic difficulties. Recognition of the various entities usually depends upon correlation of both morphologic and histopathologic features. The clinician may not be able to make a diagnosis without understanding the pathology and the microscopist may find that histologic features alone are inadequate.

Winkelman (1964)¹ included erythema nodosum, erythema induratum, nodular vasculitis, Weber-Christian disease and lipogranulomatosis subcutanea (Rothmann-Makai), pernio,** superficial thrombophlebitis, and periarteritis nodosa among the classic nodular lesions of the legs. He stated that in addition to these, several new nodular inflammations of the lower extremities have been recognized within the past two decades, such as nodular fat necrosis with pancreatic diseases, subacute migratory panniculitis, necrobiosis granulomatosis, and embolic nodules. Certain forms of necrotizing vasculitis such as the nodular dermal allergid and allergic granulomatosis should be included here also.

Classic Nodular Lesions of the Legs

Erythema Nodosum

This disorder is characterized by the *sudden appearance of tender, erythematous nodules which are raised slightly above the level of the skin*. They vary from 1 to 5 cm. in diameter and usually favor the shins, although they may occur elsewhere. The lesions are few, are all almost the same age, undergo a series of color changes, and leave no scars. They undergo involution without ulceration usually within a few weeks, although occasionally they persist longer.

The *histologic changes* are located chiefly in the upper part of the subcutaneous tissue while

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**See Test Your Word Score Page 1097.

the cutis merely shows a moderate amount of perivascular infiltrate composed predominantly of lymphocytes. In early lesions there is a scattered infiltrate in the upper part of the subcutaneous fat, which is composed mainly of neutrophils and lymphocytes. Histiocytes and eosinophils are usually present, but plasma cells are absent. As a rule the infiltrate is not heavy and is divided into numerous scattered globules among the fat cells. Abscess formation and necrosis are absent. In some instances the blood vessels are severely involved, while in others there is little or no pathologic change. Epithelioid and giant cells are usually absent in early lesions. Occasionally they are small foci composed of histiocytes lying in palisade arrangement around a small central fissure. These may be permeated by neutrophils, and since they are found in no other disease they are diagnostically important. In old lesions, giant cells, usually of the foreign body type, may occur within clusters of epithelioid cells. Caseation, however, is absent.

Erythema Induratum

Most patients with erythema induratum (necrotic nodular tuberculid or tuberculosis cutis indurativa) have a so-called chilblain type of circulation. The eruption occurs most frequently on the calves of women. *The early lesions are deep-*

seated, subcutaneous infiltrations which extend gradually to the surface, forming bluish-red plaques which ulcerate frequently. Most cases react hyperergically to tuberculin, although a few show reduced sensitivity. The presence of tubercle bacilli has been demonstrated in his-



Fig. 1 — Erythema nodosum. Acute, tender, erythematous nodules on the shins.



Fig. 2 — Erythema induratum. Deep-seated subcutaneous infiltrations usually on the calves of women.

tologic sections and by inoculation of guinea pigs. In many patients, however, no evidence of tuberculosis can be found.

In the deeper portion of the cutis and in the subcutaneous fat there is tuberculoid infiltrate. When the process in the subcutis is diffuse, the term fat-replacing infiltrate may be used. *Collections of lymphocytes, epithelioid cells, and giant cells form chiefly about the blood vessels, the layers of which are greatly thickened (endophlebitis and endarteritis).* There are nonspecific inflammatory changes in the upper portion of the cutis. The elastic and collagenous tissues are absent in the infiltrated zones.

Nodular Vasculitis

In his discussion of inflammatory lesions of the lower leg, Michelson (1952)² stated that the term was applied to both acute and chronic nodular lesions of the lower leg, which may simulate either erythema nodosum or erythema induratum, but diverge sufficiently to exclude diagnosis of either of those diseases. *The disorder is associated with some vascular disturbance, most commonly stasis.*

Histologically there is involvement of arterioles, venules, and larger vessels, especially the medium sized veins, by a granulomatous infiltrate which may extend to perivascular areas. It contains epithelioid cells, plasma cells, and foreign body giant cells, but there is no formation of tubercles. The subcutaneous tissue may be fibrotic or necrotic.

Weber-Christian Disease

The Weber-Christian syndrome was first described by Pfeifer (1892)³ and later by Gilchrist and Ketron (1916).⁴ Weber (1925),⁵ who reported the third case, created the term "relapsing nonsuppurative nodular panniculitis." Subsequently, Christian (1928)⁶ added the adjective "febrile." Clinically the disorder is characterized by the recurrent appearance of subcutaneous nodules located most commonly on the thighs and legs, but occasionally on the arms and trunk. *The lesions coalesce often to form large indurated areas.* As a rule the overlying skin shows no involvement other than mild erythema. Some-



Fig. 3 — Nodular vasculitis. Acute or chronic lesions usually associated with stasis.



Fig. 4 — Weber-Christian disease. Indurated nodules and plaques on the thighs and legs usually associated with malaise and fever.

times, however, the nodules soften and an oily liquid is discharged. Malaise and fever may herald the appearance of new lesions. After the nodules have undergone involution there may be depression of the overlying skin. Hepatomegaly and splenomegaly have been reported. Involvement of the bone marrow may result in anemia, leukopenia, and thrombocytopenia.* Fatal cases have been reported.

In this disorder as in other forms of panniculitis, disturbances of the fat are dependent on alterations of the supplying blood vessels. The small ones are usually dilated and engorged with red blood cells. Their walls may be edematous, thickened, and homogenized. In some cases, larger subcutaneous vessels show mild involvement. These changes lead to focal degeneration of fat cells and hence to outright adiponecrosis. *The necrotic foci are surrounded by a globular inflammatory infiltrate composed of neutrophils, lymphocytes, and histiocytes.* This constitutes the early (acute inflammatory) stage. In the second (lipophagic) phase there is granulomatous formation and imbibition of fat by histiocytes with foamy cytoplasm (macrophages) which dominate the infiltrate. Giant cells and eosinophils may be seen also. In the third and final (fibroblastic) stage there is swelling and homogenization of the connective tissue fibers. Fibrotic replacement of the fat finally results.

Lipogranulomatosis (Rothmann-Makai)

Lipogranulomatosis subcutanea is the term which was used by Makai (1928)⁷ to connote a form of circumscribed panniculitis, although Rothmann⁸ had described the disorder previously (1894). *It is characterized by spherical subcutaneous nodules, the size of which was described vaguely in the older literature as lentil to hazelnut, pea to cherry, and millet seed to walnut.* They average about 12 in number and are most frequently located on the lower extremities, sometimes on the trunk and occasionally on the arms. Their consistency is firm or elastic, and the overlying skin may be hyperemic or normal. Pressure elicits tenderness. The usual duration is six to 12 months, although the disorder has lasted for several years in a few instances. The nodules may disappear within a few days to a few weeks without leaving a trace. Rarely, they break

through the skin and discharge an oily fluid leaving atrophic depressions after healing occurs. Although lipogranulomatosis subcutanea is usually a disease of children, cases have occurred in middle-aged adults. Both males and females are affected. The lack of systemic symptoms, especially fever, and the fact that the lesions do not appear in crops characterize lipogranulomatosis subcutanea. These features are prominent in the Weber-Christian syndrome. The *histologic* pictures of lipogranulomatosis subcutanea and the Weber-Christian syndrome are so similar that differentiation is usually impossible.

Pernio

This disorder is characterized by erythematous nodular lesions occurring on the lower extremities as a response to cold. Female adolescents or young adults are affected most frequently. *The nodules are bluish-red and elevated, and there may be superficial ulceration.* Fifteen to 20 lesions may be present at one time and are usually located just above the ankles. Scars and hyperpigmentation occur after the nodules have healed. The course is long and progressive. The disorder occurs usually during the winter and tends to clear as warm weather approaches.

The *histopathologic features* are nondiagnostic. There may be intimal proliferation, thickening of arteriolar walls, a perivascular infiltration of lymphocytes, neutrophils, and occasional giant cells. A moderate degree of adiponecrosis is sometimes present, although there is no formation of tubercles.

Superficial Thrombophlebitis

This term implies that inflammation is associated with occlusion of a vein by a thrombus. Phlebitis, which is characterized by inflammation of the vessel wall, is not necessarily associated with the formation of a thrombus. The clinical picture depends upon the depth and size of the veins which are affected. The lower extremities are most commonly involved. *When the superficial veins are affected there are tender, erythematous, elevated nodules beneath the skin or cordlike lesions which follow the course of the vessel.* In these cases constitutional symptoms are mild or absent. There is a type of recurrent idiopathic thrombophlebitis (thrombophlebitis

*See Test Your Word Score Page 1097.

migrans) which affects males more frequently than females. In this disorder the small or medium sized veins are involved and there are multiple discrete, tender nodules which involve the legs but may be present anywhere on the body, including the abdomen. The lesions persist for one or two weeks and tend to occur in crops. As a rule the nodules are smaller than those of erythema nodosum or erythema induratum and there is no necrosis or ulceration.

Histologically there is segmental involvement of the affected vein with inflammatory changes of the walls. There may be intense proliferation of the endothelium and partial or complete occlusion of the lumen by a thrombus which contains many fibroblasts. As healing occurs the involved portion of the vein becomes fibrotic.

Periarteritis Nodosa

This disorder is characterized by kaleidoscopic polymorphism, and even though it has been known for almost a century the cause remains a mystery. A definite diagnosis is rarely made until the time of postmortem examination. The classic picture consists of a multiple-organ symptom complex with foci in the heart, kidneys, liver, intestines, muscles, brain, and sometimes the skin. The course is acute or intermittent; sometimes there are angina and arthritis in various joints. The outcome is usually fatal. In contrast to this extremely severe disease with a poor prognosis there are a few cases in which the skin has been involved exclusively. This type has a relatively benign course and may last for several years; there may be non-specific maculopapular, urticarial, or purpuric eruptions as well as those which simulate erythema nodosum or erythema multiforme. *The most characteristic cutaneous lesions of periarteritis nodosa are crops of subcutaneous nodules, especially on the extremities, although there may be livedo racemosa or multiple symmetrical gangrenous lesions.*

Most observers believe that a histologic diagnosis is possible. There is necrosis of the adventitia and media of the medium-sized arteries plus thrombosis and disruption of the elastic tissue of the vessels. There are degenerative and infiltrative changes in and surrounding the affected arteries which are located usually deep in the cutis. *The infiltrate is of a granulomatous type*

with numerous neutrophils and occasional eosinophils.

Relatively New Nodular Lesions of the Legs

Nodular Fat Necrosis with Pancreatic Diseases

Szymanski and Bluefarb (1961)⁹ called attention to this disorder. They observed five acutely ill patients who had cutaneous nodules having a characteristic fat necrosis unlike that present in any disease involving the subcutaneous adipose tissue. In all, disorder was due to disease of the pancreas. In two of the cases the cutaneous nodules preceded the appearance of abdominal symptoms. Four of the patients had acute hemorrhagic pancreatitis and one had adenocarcinoma. *There were raised erythematous cutaneous nodules which were 1 to 2 cm. in diameter (although one had "silver dollar"-sized lesions) which usually appeared on the lower extremities. The lesions were multiple but seldom reached 30 in*



Fig. 5 — Cutaneous periarteritis nodosa. The most common lesions are subcutaneous nodules and symmetrical cutaneous gangrene.

number. They were not clinically characteristic or diagnostic and simulated erythema nodosum, allergic vasculitis, or a drug reaction.

The essential *histologic changes* occurred in the subcutis without involvement of the epidermis or dermis. Foci of fat necrosis were characterized by "ghost-like" cells having thick

"shadowy" walls and no nuclei. Granular material which appeared basophilic was interpreted as dystrophic calcification. There was an inflammatory zone surrounding the foci of necrosis which consisted of neutrophils, eosinophils, lymphocytes, histiocytes, foam cells, and foreign body giant cells. The authors thought that these

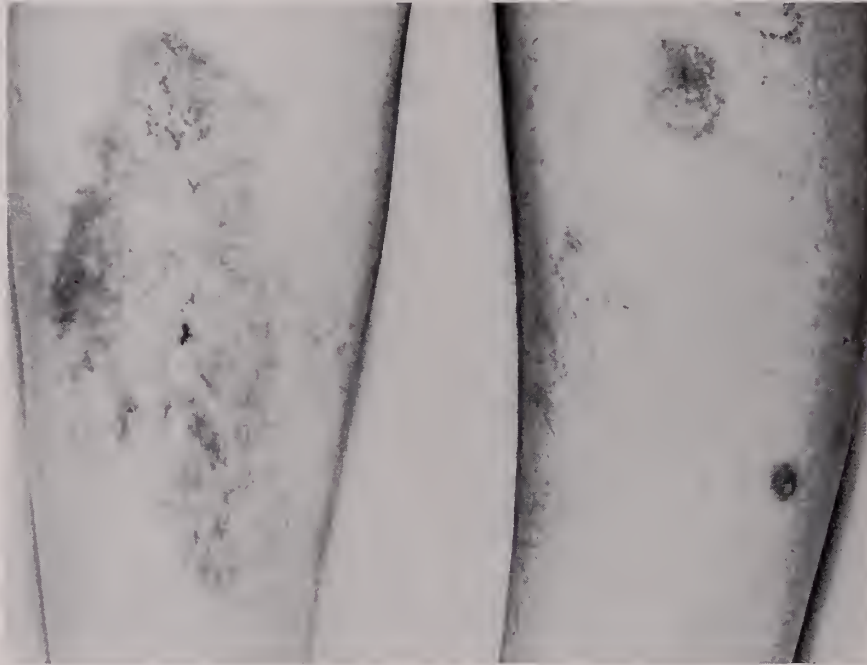


Fig. 6 — Necrobiosis granulomatosis. Sclerotic glazed plaques usually on lower portions of the legs.

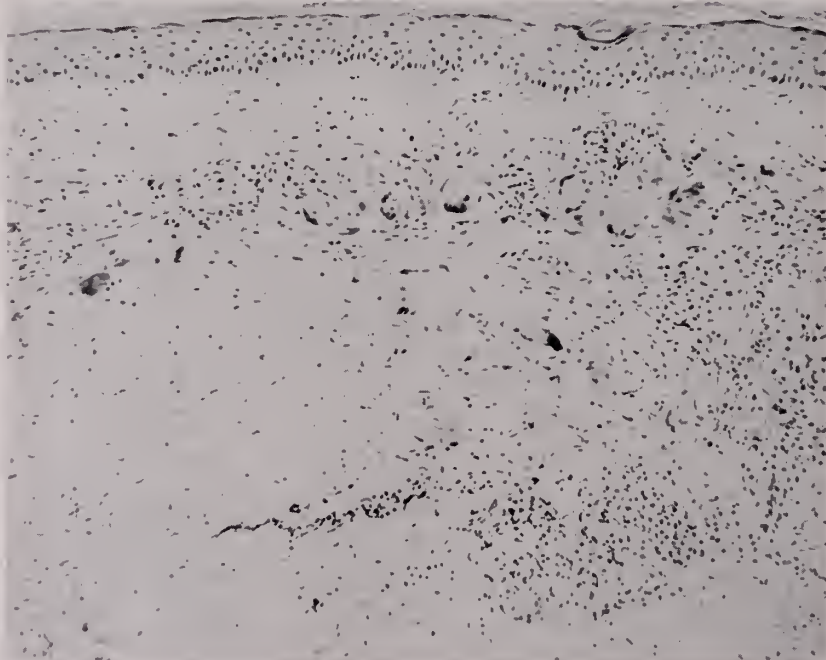


Fig. 7 — Necrobiosis granulomatosis. Tuberculoid structure in the cutis with multiple giant cells.

features were unique and pathognomonic of pancreatic disease.

Subacute Nodular Migratory Panniculitis

This disorder was described first by Vilanova and Aguade (1956),¹⁰ and more recently by Perry and Winkelmann (1964)¹¹ who reported 14 cases. Subacute nodular migratory panniculitis is characterized by discrete nodules usually on the anterolateral aspect of the legs. In the cases of Perry and Winkelmann, the disease usually started with one nodule which enlarged rapidly in one to three weeks to a diameter of 10 to 20 cm. *The progressive border of the lesion was brightly erythematous, whereas the resolving portion presented a yellowish hue.* As a rule only one leg was affected at first and pain was characteristically absent. As the lesion enlarged, it became indurated and firm and at times was almost sclerodermoid with a mottled consistency. Once fully developed the plaques persisted for periods ranging from months to three years. Most of the patients were females.

Histologically the changes were limited to the septa between the lobules of fat. Numerous histiocytes with the formation of giant cells were seen with massed aggregates up to a dozen or more between any two lobules. There was an associated mild inflammatory reaction characterized by a predominance of lymphocytes, although an occasional plasma cell was seen. There were no eosinophils. Sometimes there was extension into the lobules of fat or the adjacent dermis.

Necrobiosis Granulomatosis

Muller and Winkelmann (1966)¹² believed that this disorder was identical to granulomatosis disciformis chronica et progressiva, a disease which was described by Miescher and Leder (1948).¹³ It is similar to necrobiosis lipoidica diabetorum but differs from it by the apparent absence of diabetes and by the presence of a distinctive tuberculoid infiltrate in the dermis. Diabetes mellitus may develop later, however. *The lesions are round, sharply defined, sclerotic plaques with a glazed-porcelain sheen.* Large lesions are more irregularly shaped and oblong, and the borders are sometimes slightly elevated. The colors of the affected skin are characteristic: in early lesions there are hues of red and brown, but yellowish areas usually develop, especially

near the center of the lesions, as the disease progresses. Violaceous tints are sometimes seen at the periphery of the plaques. The lower part of the leg and ankle, particularly the pretibial area, is the most common location.

Histologically, tuberculoid structure predominates, contrasting to the findings in necrobiosis lipoidica diabetorum where there is extensive necrobiosis and significant amounts of lipid with relatively little epithelioid cell response. Exceptions have been noted however.

Embolic Nodules

Winkelmann (1964)¹ discussed this disorder. Two forms of emboli occur in the skin and may present as inflammatory nodules. In one form the emboli are from a left atrial myxoma; in the other they are from arteriosclerotic plaques. The principal source of emboli from the heart, the mural thrombus, does not produce cutaneous symptoms; but apparently an embolus from this source is so large that it blocks only larger vessels and does not reach the smaller cutaneous ones to produce changes in the skin. Winkelmann stated that single or multiple nodules may occur on the legs. His patient had pain in both calves followed

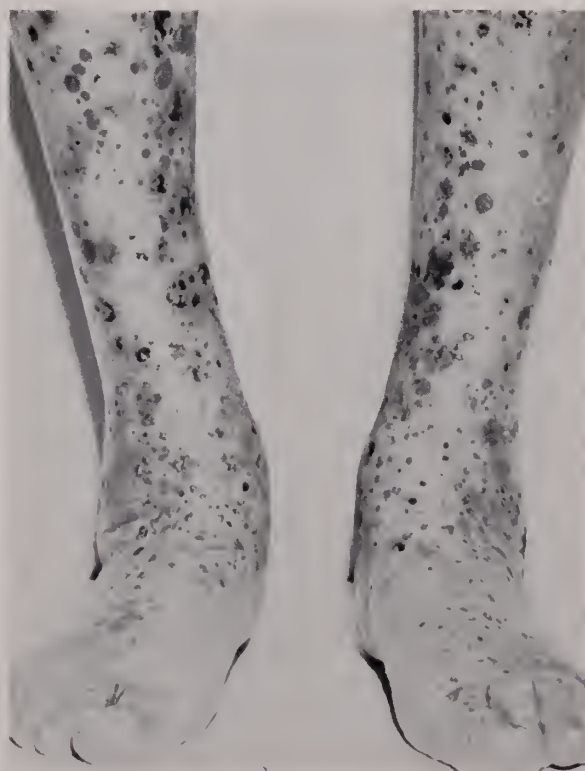


Fig. 8 — Necrotizing vasculitis. Subcutaneous nodules and purpura.

by the appearance of erythematous nodular lesions on the posterior surfaces of both thighs.

He stated that the results of the laboratory examination were normal in his patient, and review of *histologic sections* was reported to indicate vasculitis. The patient later had a new recurrence of nodular ulcerative lesions of the extremities with a febrile response. Necropsy one year later showed myxoma of the left atrium. On review of all tissue sections it was apparent that the patient had embolization to cutaneous and peripheral vessels which had produced inflammatory cutaneous lesions.

Necrotizing Vasculitis

There are several diseases which vary greatly as far as their clinical features are concerned, but which have in common the microscopic features of inflammation of the arteries in various organs, leading to hemorrhage followed by necrosis. If the arteries and capillaries are affected there may be cutaneous eruptions without interference of the general health. This is the case in the nodular dermal allergid. In the event the medium-sized arteries are involved, the term cutaneous periarteritis nodosa has been applied. If the arteries in organs other than the skin are affected, various syndromes have been described, including allergic granulomatosis, Wegner's granulomatosis, and temporal arteritis.

As the name nodular dermal allergid indicates,¹⁴ the most important lesions are round nodules from 2 to 7 mm. in diameter, some of which are almost at the level of the surrounding skin, while others project from the surface. *The lesions are indurated and well defined without any edema in the environs.* Their color may be that of normal skin, although they are usually red or purple. Besides the nodules there may be purpuric macules from 1 to 5 mm. in size and erythematopapular elements from 2 to 20 mm. in diameter, which are occasionally annular, resembling erythema multiforme. The nodular dermal allergid most frequently affects adults. The lesions occur on all parts of the body, especially on the lower extremities. They have a chronic evolution and absorb extremely slowly, except for the occasional urticarial wheals which may undergo involution in less than 48 hours. The disorder is characterized by remissions and ex-

acerbations; the latter clear within 15 to 60 days, sometimes leaving no trace and other times leaving pock-like scars and pigmentation.

Allergic Granulomatosis

Strauss, Churg, and Zak (1951)¹⁵ described a disorder which they termed allergic granulomatosis, a clinical and pathologic syndrome occurring in individuals with allergic backgrounds. It is characterized by fever, leukocytosis, eosinophilia, and pulmonary infiltrations, accompanied as a rule by manifestations of vascular, cardiac, gastrointestinal, renal, and nervous involvement. *Strauss et al. found that cutaneous lesions were frequent and consisted of erythematous maculopapular eruptions, hemorrhages varying from petechiae to extensive ecchymoses sometimes accompanied by necrosis, and subcutaneous and cutaneous nodules which persisted for weeks or even months.*

Comments

In all types of necrotizing vasculitis, there is swelling of the endothelium of the vessels, the cells of which compress each other and obliterate the lumens in some cases. There is fibrinoid necrosis of the tissue surrounding the vessel which gives rise to a sort of continuous cuff which stains pale pink and looks as though the tissue fibers had been obliterated. There is also an inflammatory infiltrate which not only lies about the area of necrosis but also extends into the surrounding tissues. This infiltrate consists mostly of neutrophils, the nuclei of which are sometimes pyknotic and may be seen lying alone and also with a fine chromatin debris. Eosinophils may be present but are not prominent.

Summary

Several old and relatively new nodular disorders of the legs have been reviewed clinically and histologically. The establishment of a new syndrome must be based on a clearly recognizable clinical pattern, a microscopic picture which is distinctive enough to justify its independence, and a course which is sufficiently characteristic to indicate the usefulness of a new term which implies differences in pathogenesis, prognosis, and treatment. Recognition of these entities thus aids the clinician.

References may be secured from the author.

None preaches better than the ant, and she says nothing. — Benjamin Franklin

Superior Mesenteric Artery

Occlusion

Successfully

Treated

by

Early

Embolectomy

IN SPITE OF a decade or more of standardized vascular surgical procedures, there have been recorded only eighteen successful superior mesenteric artery embolectomies.^{1-6,9,11-14} This low figure is not too surprising since the lesion is relatively rare, representing less than 0.5% of autopsy material¹ or between 0.02 to 0.015% of all surgical admissions⁷. The proper diagnosis is often not made until the time for successful surgical intervention has passed.

Although the sequelae of sudden superior mesenteric artery occlusion are variable, the majority end fatally without prompt surgical treatment, which requires either restoration of blood flow, resection of involved bowel segments or both. We are, therefore, compelled to make a diagnosis of the condition in its early stages and to proceed with appropriate therapy.

Anatomical Features

To a certain extent the severity of symptoms and the degree of bowel necrosis depend upon the site at which the embolus lodges. In its most common location the embolus is found distal to the origin of the middle colic artery and is also often below the take-off of the first jejunal branch. The proximal small intestine and right colon may, therefore, be nourished, for a period of time at least, via the collateral flow from these vessels, and the amount of infarcted intestine is quite variable. Conversely, if the embolus is proximal to the middle colic artery, the entire right colon and the portions of the transverse colon may be ischemic if marginal arterial collaterals from the inferior mesenteric artery are insufficient.

Clinical Features

The so-called classic history of sudden, severe, diffuse abdominal pain accompanied by nausea and vomiting developing in a patient with cardiac disease, usually atrial fibrillation, is less commonly encountered than a variety of other

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symptom complexes. Physical findings are likewise misleading in many instances, although most patients exhibit generalized abdominal tenderness, moderate distention, and initial hyperperistalsis. As the disease progresses, blood may be passed per rectum indicating mucosal necrosis, and eventually the signs of diffuse peritonitis may occur.

Standard x-ray studies of the abdomen often demonstrate the small bowel to be devoid of gas, apparently due to vigorous initial intestinal peristalsis. Nelson and Eggleston⁸ have described three characteristic x-ray signs of acute mesenteric vascular occlusion including: (1) a

"pseudotumor sign" due to excessive fluid collected in the atonic loops of bowel, (2) an ileus pattern and (3) the "rigid loop sign" due to immobile, edematous loops of bowel. Unfortunately these patterns would seem to represent actual bowel infarction and therefore should not be relied upon to help with an early diagnosis.

Surgical Features

When the diagnosis is suspected, the patient should be prepared for surgery as rapidly as possible. Preoperative hydration and digitalization

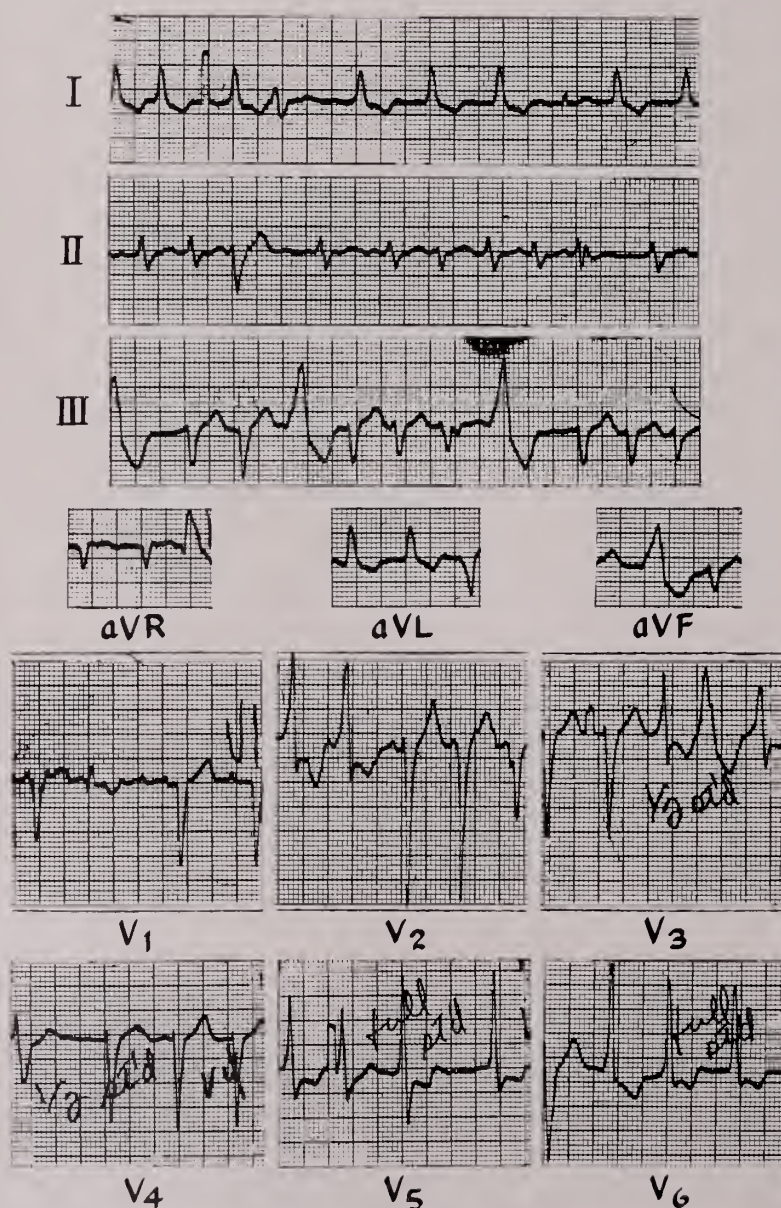


Fig. 1 — Electrocardiogram made prior to surgery.

may require a short period of delay and, if this is the case, the patient is heparinized and given antibiotics. Abdominal exploration is best carried out through a midline incision centered on the umbilicus and extended as required. Pains-taking inspection is necessary to determine the exact limits of mesenteric pulsations and ischemia. Since most emboli are lodged at or just below the middle colic branch, exposure is easily obtained by retracting the mesocolon cephalad and dissecting out the branches of the superior mesenteric artery in the root of the mesentery. An alternative approach is through the gastrocolic omentum. A longitudinal arteriotomy placed over the distal extent of the embolus allows its removal in almost all cases. A small balloon arterial catheter passed proximally may facilitate this. Distal emboli and thrombi lodged in the more peripheral arterial arcades are considerably more difficult to remove and may require retrograde flushing and manual compression to be extruded. Fortunately, early thrombotic propagation into the distal arteries is not common. In most cases it is possible to reconstruct the artery with interrupted fine sutures without a patch graft. The small bowel is then inspected, and the decision for definitive resection is made. Frankly necrotic bowel must be resected, but frequently areas of questionable viability will be encountered, and in such instances it is best to close the wound and re-explore the abdomen twenty-four hours later. However, as Rutledge⁹ has pointed out, in none of the reported cases of successful embolectomy have such "second look" operations disclosed bowel requiring resection. Immediate postoperative heparinization is probably not necessary if adequate flow has been established and may cause considerable intraperitoneal bleeding or hemorrhage from ischemic areas of bowel mucosa. However, anti-coagulation should be resumed in all patients with cardiac problems in the early postoperative period.

The following case report illustrates many of the features pertinent to the diagnosis and treatment of superior mesenteric artery embolism.

Case Report

A 77-year-old Caucasian male was admitted to Fairview-Southdale Hospital June 12, 1966, with the history of generalized abdominal pain associated with nausea and vomiting of ten hours' duration. The pain was more

intense in the periumbilical area and was constant. The patient had recently been discharged from the hospital because of generalized cardiac decompensation. At the time of his first admission, he had pulmonary and peripheral edema, pleural effusions, cardiomegaly, and an irregular rhythm. The electrocardiogram showed atrial fibrillation with rapid rate (120), numerous multifocal premature ventricular contractions, and an intraventricular conduction defect. He was digitalized and treated with a low-sodium diet, diuretics and Pronestyl. On this regimen he improved.

Physical Findings

Pertinent physical findings on the second admission showed the chest to be clear to percussion and auscultation. The heart rate was 70, the rhythm was irregular and many extrasystoles were present. No murmur was heard. The point of maximum intensity was halfway between the midclavicular line and the anterior axillary line in the fifth intercostal space. The abdomen was soft and undistended. Bowel sounds were present and normal in quality. There was tenderness in the periumbilical area on palpation with bilateral guarding. Rebound tenderness was absent, and there were no palpable masses. Rectal examination was negative. The peripheral pulses were all intact, and there was no edema.

Laboratory Studies

The white blood count was 19,500, with 83% neutrophils and 17% lymphocytes. The hemoglobin was 15.3 Gm.%. A urinalysis showed a trace of albumin and one



Fig. 2 — Abdominal flat plate illustrating complete absence of all small bowel gas.

plus white blood cells/hpf. Two-hour urine amylase was 254 units. Serum electrolytes were within normal limits. The electrocardiogram was essentially unchanged from the previous admission except for more frequent premature ventricular contractions (Figure 1). The chest x-ray showed a slightly enlarged heart, although smaller than on the previous admission. Abdominal films showed a complete absence of small bowel gas (Figure 2).



Fig. 3 — Removal of embolus from superior mesenteric artery.



Fig. 4 — Normal postoperative small bowel mucosal pattern.

Surgical Findings

A diagnosis of acute abdomen, probably on the basis of mesenteric artery embolism or thrombosis, was made and the patient underwent laparotomy. The superior mesenteric artery was found to be pulseless beyond the takeoff of the middle colic artery. The first portion of the jejunum was normal, but two feet beyond the ligament of Treitz there was a dilated, edematous, pale segment of jejunum approximately 12 inches in length which had no peristalsis. The remainder of the small intestine was normal in color and had adequate peristalsis, although no arterial pulsations were present in the mesentery supplying this area. The superior mesenteric artery was opened at the point of occlusion and a well-organized embolus was removed (Figure 3). Following closure of the artery, pulsations were felt at the level of the major arcade in the mesentery, but not in the more distal branches of the jejunum or ileum. The color of the involved segment of bowel improved and active peristalsis returned. The abdomen was closed, and it was decided to re-explore the patient 24 hours later in order to determine if any demarcation of bowel had occurred. On re-exploration, the 12-inch segment of proximal jejunum was slightly boggy, but exhibited peristalsis and a normal color. The remainder of the bowel appeared quite normal except for numerous ecchymotic areas. Following surgery the patient had an uneventful, although prolonged recovery. Upon resumption of a normal diet he had some diarrhea and postprandial periumbilical cramping, which lasted for one month.

Follow-up

At subsequent follow-up examinations the patient has demonstrated no abnormal bowel function. A small bowel x-ray showed a normal mucosal pattern (Figure 4). There is no evidence of any malabsorption or any dietary intolerance. He continues to have atrial fibrillation but is well compensated on digitalis.

Comment

Although the abdominal findings were not dramatically pronounced on initial examination in this particular patient, when considered in the light of recent congestive heart failure and atrial fibrillation, the entire picture suggested acute superior mesenteric artery occlusion. Early exploration and embolectomy allowed restoration of blood flow before actual intestinal infarction developed.

Immediate postoperative heparinization was begun, but this was associated with the presence of considerable intraperitoneal bleeding at the time of re-exploration, presumably from the area of mesenteric dissection, and therefore was discontinued.

After an initial period of nutritional adjust-

ment of about one month, the patient ate normally, and there has been no clinical evidence of malabsorption. Furthermore, the small bowel pattern was noted to be entirely normal. We feel this is fortunate, because several authors have described chronic malabsorption states in patients surviving superior mesenteric artery embolotomy^{10,12}.

Summary and Conclusions

Successful superior mesenteric artery embol-

tomies have been reported infrequently. Constant vigilance is required to select patients with the findings and history suggestive of superior mesenteric artery occlusion and submit them to early abdominal exploration if the sequelae of bowel necrosis are to be avoided. A case history has been included which illustrates certain pertinent diagnostic features and outlines the therapeutic measures which allowed a successful result following early superior mesenteric artery embolotomy.

References

1. Atwell, R. B.: Superior Mesenteric Artery Embolotomy. *Surg Gynec Obstet* 112:257-258, 1961.
2. Baue, A. E., Austen, W. G.: Superior Mesenteric Artery Embolism. *Surg Gynec Obstet* 116:4:474, 1963.
3. Bergan, J. J., Hoehn, J. G.: Superior Mesenteric Artery Embolotomy. *JAMA*, 188:10:935, 1964.
4. Bohn, G. L., Carroll, K. J.: Superior Mesenteric Embolotomy. *Gut*, 5:4:363, 1964.
5. Hardy, E. G.: *Brit Med J* 5346, June 22, 1963.
6. Mathiesen, F. R.: Acute Mesenteric Vascular Occlusion Treated With Embolotomy. *Acta Chir Scand* 126:3:275, 1963.
7. Morse, L. J., Krynski, B., Mukeen, T. T.: Superior Mesenteric Vascular Occlusion. *Amer J Surg* 93: 788, 1957.
8. Nelson, S. W., Eggleston, W.: Findings on Plain Roentgenograms of the Abdomen Associated with Mesenteric Vascular Occlusion with a Possible New Sign of Mesenteric Venous Thrombosis. *Amer J Roentgen* 83:886, 1960.
9. Rutledge, R. H.: Superior Mesenteric Artery Embolotomy: Review of the Literature and Case Report. *Ann Surg* 159:4:529, 1964.
10. Shaw, R. S., Maynard, E. P.: Acute and Chronic Thrombosis of the Mesenteric Arteries Associated with Malabsorption. *N Eng J Med* 258:18:874, 1958.
11. Shaw, R. S., Rutledge, R. H.: Superior Mesenteric Artery Embolotomy in the Treatment of Massive Mesenteric Infarction. *New Eng J Med* 257:13:595, 1957.
12. Weaver, J. P. A., Anderson, J., Hoddon, R. W. T.: Recovery of Intestinal Function After Successful Superior Mesenteric Artery Embolotomy. *Brit J Surg* 52:6:440, 1965.
13. Zuidema, G. D., Reed, D., Turcotte, J. G., Fry, W. J.: Superior Mesenteric Artery Embolotomy. *Ann Surg* 159:4:548, 1964.

The Physician's Image In Ancient India

To the sick man the doctor is a father: to the man in health a friend: the sickness passed and health restored, a preserver.

Without practical training and merely by hearing lectures and by the repetition of discourses, a pupil is like an ass with a burden of sandalwood, for he knows its weight but not its value.

He who knows only one branch of his art is like a bird with one wing. . . . He who is versed only in books will be alarmed and confused, like a coward on a battlefield, when confronted with active disease; he who rashly engages in practice without previous study of written science is entitled to no respect from the best of mankind, and merits punishment from the king; but he who combines reading with experience proceeds safely and surely like a chariot on two wheels.

The physician, the patient, the medicine and the nurse are the four feet of medicine upon which the cure depends. When three of these are as they should be, then by their aid the exertions of the fourth, the physician, are of effect, and he can cure a sore disease in a short time. But without the physician the other three are useless. . . . A good physician can cure a patient alone, just as a pilot can steer a boat to land without sailors.*

*The Code of Manu (400 B.C.—200 A.D.)

Your Health—Mr. President!

Zachary Taylor (1784-1850)

A Bowl of Cherries

Did our twelfth president, Zachary Taylor, die of overeating on cherries?

Throughout childhood and youth Zachary was healthy and hardy; not until military service in the Indian and Mexican Wars was his constitutional integrity violated and perhaps permanently impaired by the acute intestinal infection so perniciously endemic to the appallingly unsanitary army camps of that era. Of his second febrile attack with dysentery he said: "The fever confined me to my bed for near two weeks, when so many was dying around me who I could render no service nor even pay a friendly visit. . . But after taking a large quantity of active medicine principally calomel, and living altogether on hot drinks the disease was subdued, but left me very much debilitated."

Though needlessly rash and reckless throughout his military campaigns Taylor was on the receiving end of bullets only once. From one of his biographies we learn: "One ball passed through his left sleeve above the elbow in the part between the arm and the body, making a large hole where it went in and where it came out. . . It cut through both of his shirts and grazed the skin of his arm. Another entered the breast of his coat, cut through the lining for several inches, and came out at the button hole, tearing it away."

During Taylor's occupancy of the White House his otherwise personable appearance was somewhat marred by undue obesity; for his height of five feet eight inches he weighed 200 pounds. Rather striking also was a strabismus, that impelled him to keep one eye partially shut while in close conversational proximity to anyone.

At an Independence Day celebration in 1850, after Taylor had stood and walked under a blazing sun too long, he became overheated and inordinately thirsty; whereupon he drank vast amounts of ice-cold water, then ate huge quantities of cherries, finishing off his binge with more ice-cold water and milk. As if that were not more than sufficient he topped off his dinner that same evening with more ice-cold water and more fruit, principally cherries, even at the protest of his doctor who was present at the meal. The inevitable result: severe cramps and diarrhea that abated temporarily and slightly—only to resume more violently with vomiting of watery bile and then demise. Standing helpless and defeated at the bedside the several attending physicians debated the cause of death with no consensus; and no autopsy was conducted to establish which of the dissenting opinions presented the correct diagnosis of Taylor's fatal disease.

However, the myth promptly disseminated, gaining momentum and credence, that Zachary Taylor's death was due to overconsumption of cherries: a prime example of how the post-hoc-ergo-propter-hoc fallacy can generate an irrefutable national legend.*

Editor's Note: With unrelenting vomiting and diarrhea the modern doctor would no doubt have made a diagnosis of massive water loss and an electrolyte imbalance as a contributory cause of death.

*With acknowledgments to Karl C. Wold, M.D.: Mr. President—How Is Your Health? 1948.

Solitary Myeloma of Bone

Report of a Case 13 Years After Diagnosis

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SOLITARY MYELOMA of bone, or plasmacytoma,** is extremely rare. When diagnosed as such, it is frequently only the precursor of generalized myeloma. True solitary myeloma, if properly treated, follows a benign course and has a good prognosis. We agree with Carson and associates³ that if the so-called solitary lesion is followed long enough, it will show evidence of generalization, while the true solitary myeloma is rare. In 1941, Willis¹⁴ reported only 13 genuine cases in a review of the literature. By 1964, Cohen *et al.*⁵ had added 13 more cases which met the criteria of the true solitary lesion.

We wish to report a case in which, although the lesion was diagnosed in 1952, the tumor had apparently begun its course in 1951.

Case History

A 43-year-old white man was first seen in May, 1952. In January, 1951, he had strained his back by lifting a motor. This had resulted in mild low-back distress until March, 1951, when he noticed pain extending down the left leg along the posterolateral aspect to the ankle. Coughing and sneezing aggravated this pain. About six months later he consulted a chiropractor and received multiple manipulations, with apparent relief of pain, although he had been unable to work during the period of treatment.

He had also sustained a severe back injury in 1931, which resulted in a compression fracture of D-8, from which he had recovered.

Physical Findings.

He walked with a stiff, guarded, forward-leaning gait. His spine was rigid and straight and the low-back motion was about 25 per cent of normal. There was a 4.5 cm. atrophy of the left thigh, although the calves were symmetrical. There were no other physical abnormalities noted.

X-ray Findings

Roentgenograms of the lumbar part of the spinal column showed a large osteolytic lesion involving L-3 (Figure 1). The process extended mostly over the right side of the vertebral body and posteriorly, with destruction of the right pedicle and expansion of the most medial portion of the right transverse process. The

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**See Test Your Word Score Page 1097.

lamina and the anterior portion of the spinous process were also involved. Its appearance was that of a mixture of an expanding and cystic lesion showing some trabeculation. The roentgenograms were interpreted as indicating a growth that was probably primary; but a metastatic lesion could not be ruled out.

Films taken elsewhere in 1931 and in September, 1951, (Figure 2) were examined. No lesion was present in 1931, although there was evidence of pathologic changes in the 1951 films, which showed a definite osteolytic lesion in the right side of L-3. The lesion had grown considerably since that date.

Roentgenologic survey of the rest of the skeleton was negative.

Laboratory Findings

Laboratory studies included hemoglobin, red and white-blood cell count, urinalysis and sedimentation rate. All were normal. Within a month after this first examination, needle biopsy was attempted without success. This was followed by laminectomy and removal of all the grossly visible tumor.

The tissue was comprised of sheets of densely packed plasma cells, quite regular and mature in type (Figure 3). The histologic diagnosis was myeloma.

Postoperative Course

The patient did well postoperatively and received a

full course of radiation therapy. He has been seen periodically in our clinic since.

In January, 1953, he reported some discomfort in the wound area. Roentgenograms showed the surgical defect without any definite evidence of bone regeneration (Figure 4). In December, 1958, he denied any distress and was working without difficulty. He had an excellent range of back motion with no apparent guarding. Roentgenograms of the chest and spine revealed no evidence of any new lesion. In October, 1964, he was still symptom-free. Laboratory studies showed a total serum protein of 8.1 Gm. per 100 ml., with albumin 5.5 Gm. and globulin 2.6 Gm.; serum calcium was 11.5 mg. per 100 ml. Serum electrophoresis showed a normal pattern; bone-marrow examination revealed no evidence of dyscrasia.

The patient was last seen in October, 1965, at which time roentgenograms showed bone regeneration of L-3 without evidence of any active lesion. (Figure 5). The patient denied any pain referable to the involved area.

Comment

Although the lesion in our patient was not diagnosed definitively until May, 1952, roentgenograms in September, 1951 (Figure 2), indicate the lesion was then apparent. The patient can

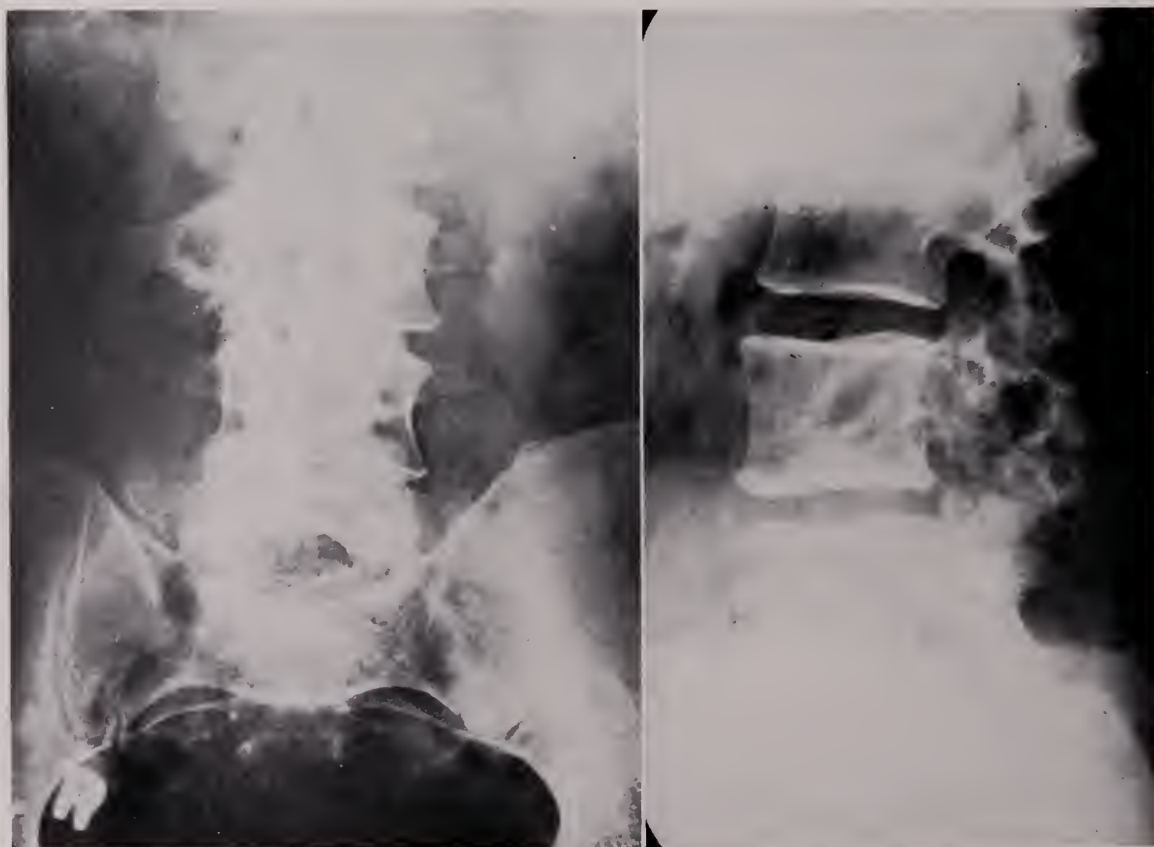


Fig. 1—Obvious involvement of the right side of vertebral body, including lamina and transverse process.



Fig. 2—Earliest available evidence of pathology at right side of L-3 (1951).

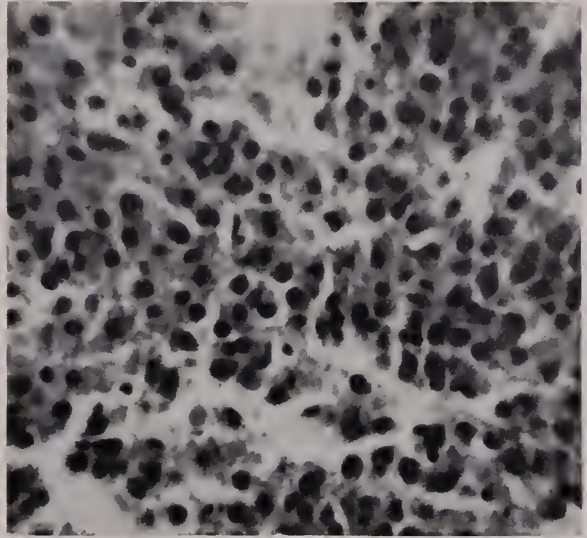


Fig. 3—Note almost total replacement of normal cells by densely packed mature plasma cells.



Fig. 4—Roentgenogram 6 months postoperatively and postirradiation shows no definite bone regeneration.

thus be said to be alive and well more than 14 years after his first symptoms appeared.

Some disagreement exists in the literature regarding this entity. Since some long-term solitary lesions eventually generalize, some question occurs whether all solitary lesions are precursors of multiple myeloma.

Bichel and Kirketerp,² and Christopherson and Miller⁴ believed that a three-year survival rate was sufficient to justify the diagnosis; but many lesions have disseminated after three years. Raven and Willis¹¹ stated that a one-year follow-up with negative roentgenologic findings should be ample. Pasternack and Waugh¹⁰ reserved the term "true" solitary myeloma for lesions showing no recurrence or secondary foci for four to 10 years after diagnosis.

In our case only one bone-marrow examination was made, although some authors believe serial bone aspirations should be done. However, Lichtenstein and Jaffe⁹ found that negative bone marrows and even a negative autopsy report might not rule out other foci of myeloma. We believe that such examination done this late in

our post-diagnosis period would help considerably to corroborate or disprove the original diagnosis. While we agree with Bichel and Kirketerp² that bone-marrow studies are important in diagnosing this condition, we also find a case reported by Baitz and Kyle¹ in which myeloma developed after a 40-year history of osteomyelitis; bone-marrow examinations, among other tests, were negative despite the rapid generalization of the disease which preceded the death of the patient.

One skeletal survey was made on our patient; this was immediately preoperative. The variability of skeletal spreading either locally or generalized is well seen in one of the cases reported by Kaye *et al.*⁸ in which skeletal invasion was evident 12 years after the lesion was first diagnosed. Skeletal invasion produces symptoms more often than not, and since our patient has been symptom-free since at least 1958, no such study has been done except for thoracic roentgenograms at each visit. Three years postoperatively, skull roentgenograms were negative.

The two most interesting facets of such tumors are their rarity and the different approaches to the

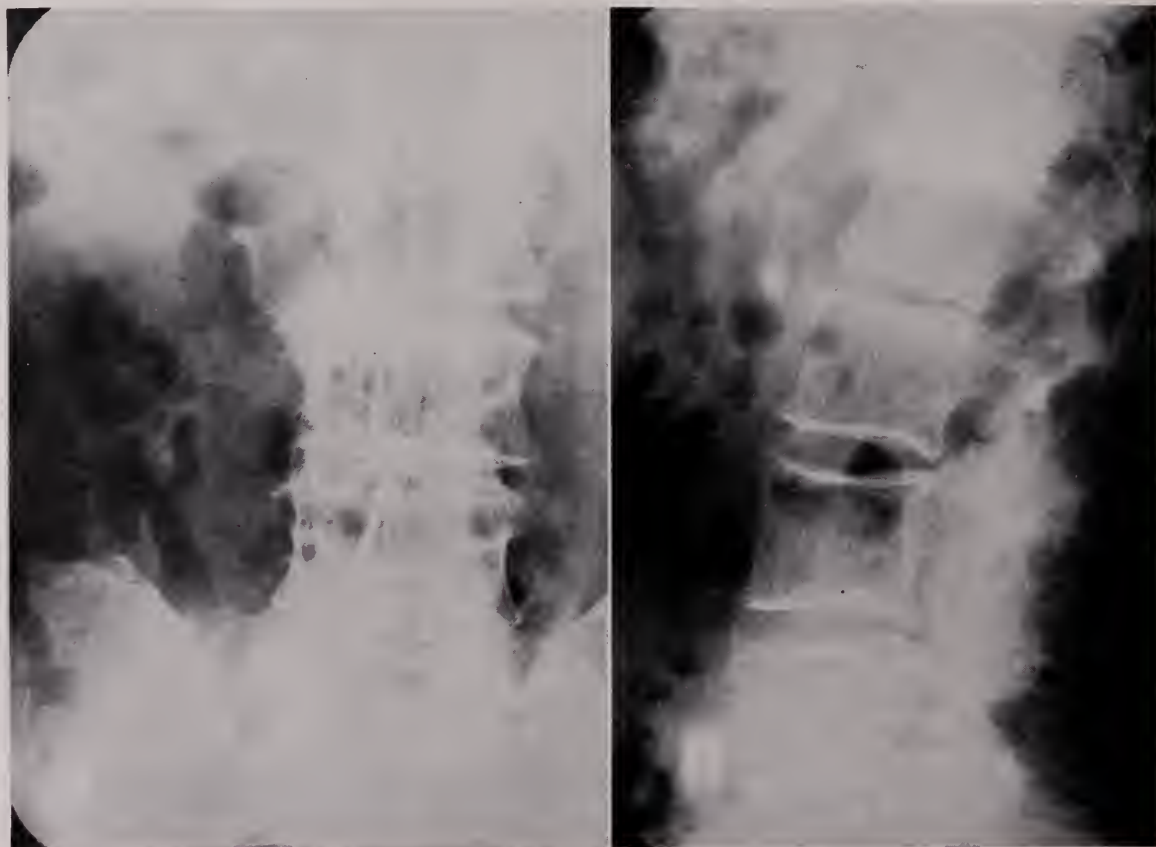


Fig. 5—Roentgenogram 13 years postoperative and postirradiation shows bone regeneration without evidence of recurrence.

subject in the literature. If there exists a true "solitary" benign lesion without evidence of generalization, the number of reported cases is extremely small. Carson and co-workers,³ in reviewing 90 cases, accepted this rarity as an entity but stated that, given a long enough time, most of the patients will show diffuse plasma-cell myeloma. As recently as 1964, Cohen *et al.*⁵ reported on a patient in whom disseminated myeloma developed 21 years after the original "benign" lesion had been excised.

The approaches to the subject vary considerably in the literature. Our patient was not tested for Bence Jones proteinuria. Cohen *et al.*⁵ demonstrated that the presence of this protein in the urine does not necessarily imply brief survival. One of their patients who had a normal bone marrow at the time of the original diagnosis also had Bence Jones proteinuria but survived for 10 years. Interestingly, he died of local extension of a sacral myeloma without evidence of generalization at autopsy.

Weiner,¹³ in reviewing 60 cases, studied serum-protein changes by electrophoresis and found that these, as well as Bence Jones proteinuria, were seen only occasionally in plasmacytoma of bone. The serum electrophoretic pattern in our patient was normal.

The relationship between multiple myeloma and the true plasmacytoma remains only partially answered. Christopher and Miller⁴ stated emphatically that there was no relationship. Johnson and Meader⁷ reported a case with two different foci of myeloma with identical microscopic characteristics, indicating the possibility that the tumor was multicentric and yet benign. Their patient was alive six years after discovery of the lesions. They suggested the possible distinction between the two entities, defining the so-called solitary myeloma as nothing more than reactive hyperplasia of the marrow involving the cytoplasmic characteristics of the histiocytes;^{*} this would serve to make the differentiation from true

myeloma, either solitary or multiple. However, they admitted the possibility that this hyperplasia may undergo sarcomatous changes and that predictions as to behavior of benign solitary myelomas should be made cautiously.

Ritz and Meyer¹² also agreed that the relationship between solitary and multiple myeloma should be clarified. They suggested the term "plasmacytoma" be used for those lesions in which the outcome is in doubt, reserving the terms "benign" or "malignant" plasmacytoma for those with distinct characteristics. They did not, however, elaborate on the length of time which should elapse before determination of the benignancy.

The same spectrum of approaches is apparent in the various roentgenograms offered for examination. While Jacobson *et al.*⁶ considered destruction of the pedicle as characteristic of metastatic carcinoma or a very late sign in myeloma, Cohen and co-workers⁵ found pedicle destruction in 20 of their 55 cases of isolated vertebral myelomas.

Conclusions

While most of the lesions described are osteolytic, roentgenographic diagnoses of metastatic and giant-cell tumors, aneurysmal bone cyst and Ewing's sarcoma have been made in an attempt to offer prognostic help. This attempt has not been particularly rewarding and we feel, as many do, that differential diagnosis is not possible without biopsy or other supplementary studies or both.

One point of common agreement emerges: treatment of these lesions is biopsy followed by well-conducted radiation therapy. All factors being equal, this approach should bring about a benign course and a good prognosis.

Upon review of the literature and comparison of the symptomatology, definitive diagnosis, post-operative course and 14-year survival record, we believe our case to be that of a benign solitary myeloma.

References

1. Baitz, T., and Kyle, R. A.: Solitary Myeloma in Chronic Osteomyelitis. Report of a Case. *Arch Intern Med* 113:872, 1964.
2. Bichel, J., and Kirketerp, P.: Notes on Myeloma. *Acta Radiol* 19:487, 1938.
- 3-14—May be secured from the author or the reprints.

*See Test Your Word Score Page 1097.

Conceit may puff a man up, but never prop him up.

—*Ruskin*

The Minnesota State Bird*

A few years ago, after much debate, the common loon was named the Minnesota state bird. To many the loon meant only a bird with a weird cry which had given rise to such expressions as "crazy as a loon." However, to many dedicated lovers of wild life the loon represents a true symbol of the wilderness. Dr. W. J. Breckenridge, Dean of Minnesota Wild Life Students and Teachers, has been quoted in part as saying, "The loon expresses the essence of unrestrained wildness and seems to put the stamp of genuineness on a north country setting."

Last May during three days of bass fishing in a sheltered bay of Long Lake near Park Rapids, my fishing partner, Paul Wilson, and I made the acquaintance of the nesting loon of this cover picture. At first she would leave the nest when we were 50 to 75 yards away, making wild and angry cries, and further tried to distract us by rearing up on her tail and throwing out her chest with a great flapping of wings. As we drifted on fishing, she would slowly return and with awkward waddling resume her place on the nest. It is amazing that one of the world's greatest swimmers can be so helpless on land. After several fishing trips she finally decided to accept or ignore us.

On a particularly beautiful morning as Paul worked the boat toward the nest, I took pictures at various distances without disturbing Mrs. Loon. The picture presented was taken as a 35-mm. slide at a distance of twelve feet on Kodachrome II using a 135 mm. lens.

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*See May Cover of MINNESOTA MEDICINE.

Medical Men on Postage Stamps

Rene Laennec (1781-1826) was a French physician, author of a book on chest diseases, and inventor of the stethoscope. A one-foot-long wooden cylinder constituted Laennec's first crude instrument for auscultation; with it he listened to mysterious chest wheezes, rattles, and whistles which at the time confounded him but which he later was able through autopsies to correlate with the disorders that had produced them. In 1952 France acknowledged its debt to him by issuing a postage stamp in his honor.

Federico Roldan (1864-1942) was a Cuban physician who introduced radiotherapy and physiotherapy to his native country. In commemoration Cuba issued a postage stamp honoring him in 1958.

Ancient Greeks in Medicine*

ARETAEUS (1st century A.D.) described asthma, tetanus, epilepsy, diphtheria, hysteria, satyriasis, warned against excess of bloodletting, seems to have understood the direction of the blood-flow in the veins, and was the author of the first systematic account of diabetes.

ASCLEPIADES (1st century B.C.) was the first who definitely divided disease into acute and chronic; he described malaria, catalepsy, frenzy and lethargy, and treated the insane with gentleness, sunlight, music and song.

HELIODORUS (3rd century A.D.) wrote on operative treatment of hernia, stricture, resections, flap and circular amputations, bandaging, probing injuries to the skull and torsion of blood vessels.

SORANUS (98-138 A.D.) stands out as the first specialist in diseases of women and children.**

*See Minnesota Med 50:1015, 1967.

**Massengill, S. E.: A Sketch of Medicine and Pharmacy, The S. E. Massengill Co., Bristol Tenn.-Va.

Thrombocytopenic Purpura and Intra-Uterine Growth Retardation

*of
the
Newborn
Following
Maternal
Rubella*

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RECENT PAPERS have reported purpura, thrombocytopenia, intra-uterine growth retardation, hepatosplenomegaly, bone changes, and other anomalies as new features of the rubella syndrome.^{1,2,3,4} The question arises whether these are new manifestations due to a change in pathogenicity of the virus or whether these features may previously have been missed. This report of three cases from the years 1958 and 1959 demonstrates that such complications occurred prior to the recent epidemic.

Case Reports

Case 1

A 23-year-old mother was seen by her family physician during the sixth week of pregnancy and was diagnosed to have German measles. The pregnancy was otherwise uncomplicated. Her last menstrual period had been on 4.27.57, the date of expected confinement was 2.2.58, and the birth occurred on 1.16.58 at 38 weeks of gestation. Delivery was normal. Physical examination revealed a 3 lb., 14 oz. boy; length 17½ inches, head circumference 12 inches, chest circumference 11½ inches. Reddish-blue hemorrhagic macular areas from pinpoint size to 3 to 4 mm. in diameter were present over the entire body. They did not fade on pressure and were typically purpuric. No new lesions appeared and by the twelfth day the lesions had almost completely faded. At two weeks of age a short, rough systolic murmur had developed which gradually became louder. A presumptive diagnosis of interventricular septal defect was made. The murmur later disappeared. At the age of four weeks the baby developed coarse tremors which persisted for several weeks. When he was two months old, cloudiness of the cornea of both eyes was noted and a diagnosis of congenital glaucoma was made. Goniotomies were performed on both eyes in May and December 1958. Cataract developed in the right eye; good vision (20/50) was achieved in the left eye.

Repeated platelet counts showed significant reduction: at the age of 24 hours the count was 77,000/ml³, at the age of four days 40,000/ml³, at six weeks 149,000/ml³, at two months 138,000/ml³, at four months 133,000/ml³, and at five months 160,000/ml³.

An interval history was obtained when we had an opportunity to see him again in December 1964 at age 6 11/12 years. Psychometric testing in January 1960 on the Cottrel Infant Scale had shown a chronological age of two, a mental age of two, an I.Q. of 100; and on 6.20.62 a Stanford-Binet I.Q. was 109+. In July 1963 he had bilateral heel cord lengthening. In November 1963 he had bilateral tenotomies of the adductor muscles with obturator neurectomy.

Although he spoke slowly with a definite though not severe defect and mispronounced some words, he could be easily understood. He was friendly and cooperative.

Physical examination showed his weight to be 51 pounds, his height 46½ inches, his head circumference 49 cm. The deciduous teeth were short and appeared worn, with yellow discoloration of the enamel. There was no heart murmur. He had severe spasticity of the lower extremities. He walked well with crutches, but when walking alone he moved his legs mainly by stiffening and rotating his hips. Coordination of his hands was good. He attended special school.

Case 2

A 22-year-old nurse had her first successful pregnancy after two miscarriages. Her last menstrual period had been on 3.19.59; her expected date of confinement was 12.22.59.

Rubella was diagnosed on 4.23.59 by her obstetrician and a dermatologist. Pregnancy, labor and delivery were otherwise normal. The patient, a girl, was born on 12.17.59 at 40 weeks of gestation, weighing 4 pounds, 15½ ounces; length 19 inches, head circumference 12½ inches, chest circumference 12 inches. There was a generalized eruption of small macular blue-red spots which did not fade on pressure, characteristic of purpura. The left eye showed microphthalmia and a cataract. There was a grade two apical systolic murmur which had disappeared by the fourth day.

Repeated platelet counts were significant: on the first day of life duplicate counts were 37,000/ml³. and 34,000/ml³.; at one month the platelets had risen to 171,000/ml³. and showed conspicuous pleomorphism with many giant forms; at 4½ months the count was 235,000/ml³. and the platelets were morphologically normal.

During the first year of life the child had frequent upper respiratory infections and recurrent purulent otitis media. In July 1960 and January 1961 dissection of the second pupillary membrane of the microphthalmic left eye was done. Examination of the right eye showed a salt-and-pepper type fundus and a disc-sized area of an old choroiditis just temporal to the right macula.

At five months she weighed 12 lbs., measured 24½ inches with head and chest circumference of 37 cm. each. In April 1965 at the age of six years, she weighed 29 pounds, her measured height was 40¼ inches with head and chest circumferences of 46 cm.

She sat at seven months, took a few steps alone and walked around furniture at 12½ months. She was a bright, pretty, petite little girl, with a normal intelligence when tested with a Stanford-Binet Form LM: at C.A. 5-7 (M. A. 6-2, I.Q. 112). The Binet was corroborated by the Goodenough test and history from the mother.

Hearing tests showed a very slight high frequency sensory hearing loss, so slight that it had no effect on her speech and language behavior. The results of the Peabody Picture vocabulary test indicated language development well in advance of her chronological age.

Case 3

During the second month of suspected pregnancy

a 41-year-old mother contracted what was thought to be rubella. She had a rash, sore eyes, and a fever. She was seen by her family physician who took a "rabbit" test which confirmed the pregnancy. Except for a renal infection during the last trimester the pregnancy was normal. Her last menstrual period had been 1.27.59; her date of expected confinement was 11.4.59. The infant was born at 42 weeks of gestation on 11.17.59 after normal labor and delivery. The placenta showed multiple infarcts. The infant weighed 3 pounds, 1½ ounces; length 16½ inches; head 12¼, chest 8¼ inches. There was a generalized purpuric macular rash. The right testis was not palpable; the left testis was in the inguinal canal. There was a grade 2 systolic apical murmur which disappeared at two weeks. The eyes appeared normal.

Significant laboratory findings were: the platelet count on 12.2.59 was 100,000/ml³.; on 12.16.59 the platelets were markedly pleomorphic with a count of 104,000/ml³., and on 12.28.59 the count was 224,000/ml³.

At discharge when two months old the infant weighed 5 pounds, 4½ ounces. At nine months of age he appeared grossly retarded (weight 13 pounds, 2 ounces, height 68 inches, head 42 cm., chest 37 cm.). His highest level of achievement was to roll over, but he was beginning to imitate sounds and was able to hear. His head was of the long, narrow scaphocephalic type. The fontanel and coronal sutures were open. His back tended to be arched, his fists clenched. He was unable to sit alone but stood with support in a typical six-month pattern with the feet plantar flexed. His deep tendon reflexes were brisk, Babinskis were bilaterally positive, Moro was absent.

At the age of two years he started to walk around furniture. He used his upper extremities and his hands quite well but still arched his back and had marked spasticity in the lower extremities. His measurements were: weight 17½ pounds, height 83 cm., head 45.3 cm., chest 43 cm. At age 3¼ years he weighed 22 pounds, 8 ounces, and measured 36½ inches; but he still did not walk alone. Psychometric testing at C.A. 3.6 showed M.A. 1.9, I. Q. 50 on the Cottrell Infant Intelligence Scale. His hearing was apparently grossly normal. His speech was poor; he had difficulties with coordination, jaw, lip and tongue movement.

Discussion

That the intra-uterine growth retardation in these patients was striking, fits well with Warkany's concept.⁵ The children's birth weights were much less than expected for these gestational ages: 3 pounds, 14 ounces at 38 weeks, 4 pounds, 15 ounces at 40 weeks, and 3 pounds, 1½ ounces at 42 weeks in the three cases. Their head circumferences were also small for their gestational age; but the measurements were near to the expected mean values for the birth weight. None of the children has "caught up" with his normal siblings. However, when last seen one

was near the mean in height and weight, and another had a fairly normal height. Otherwise, height, weight, head circumference were grossly abnormal, generally below the 3rd percentile. Two of the children are spastic; one with severe spasticity is also markedly retarded mentally.

The purpura at birth was striking. In every case it was initially thought to be unrelated to the history of maternal rubella. Two infants had platelet counts checked within 24 hours; these were significantly depressed. The platelets in the third child were not checked until 14 days of age when the count was 100,000/ml.³ and the platelets were markedly pleomorphic.

All three children had loud heart murmurs during the neonatal period, which disappeared early. This might represent closure of a patent ductus or patent atrioventricular canal.

More recently described features of the rubella syndrome were probably missed in our cases. X-rays of the long bones were not taken. There were no notes on the size of the liver or spleen. However, thrombopenic purpura and intra-uterine growth retardation were recognized as features of the syndrome.

The early work with rubella syndrome and its traditional involvement of eyes, ears, heart and teeth was done in older children. The rather transient and harmless purpura, "bruising from birth," could have been easily passed over and forgotten. Only in recent epidemics when the diagnosis of rubella syndrome was made at birth, did the relation of purpura, bone changes, enlarged liver and spleen to the rubella syndrome become obvious. The fact that thrombocytopenic purpura did occur in three newborns in 1958-1959 suggests that the more recently described features of the rubella syndrome were missed in the past and not that the virulence of the virus or the character of the diseases changed.

Summary

Three cases of the rubella syndrome of the newborn with purpura, thrombocytopenia, and intra-uterine growth retardation that occurred in 1958 and 1959 are reported.

The author wishes to express his appreciation to the referring physician of each of the three cases: Calvin Elrod, M.D., Charles A. Friend, M.D., and Joseph I. Hamel, M.D.

References

1. Rudolph, A. J., Yow, M. D., Phillips, C. A., Desmond, M. M., Blattner, R. J., and Melnick, J. L.: Transplacental Rubella Infection in Newly Born Infants. *JAMA* 191:843, 1965.
2. Banatvala, J. E., Horstmann, D. M., Payne, M. C., and Gluck, L.: Rubella Syndrome and Thrombocytopenic Purpura in Newborn Infants. *New Eng J Med* 273:474, 1965.
3. Rausen, A. R., London, R. D., Mizrahi, A., Cooper, L. Z.: Generalized Bone Changes and Thrombocytopenic Purpura in Association with Intra-uterine Rubella, *Pediatrics* 36:264, 1965.
4. Cochran, W. D., Cornfield, M., Friedberg, D.: Congenital Rubella and Thrombocytopenia, *Pediatrics* 36:268, 1965.
5. Warkany, J., Monroe, B. B., and Sutherland, B. S.: Intra-uterine Growth Retardation, *Amer J Dis Child* 102:249, 1961.

Minnesota Medicine Cover Photographs

In order to encourage more physicians to submit color slides for use on the cover of MINNESOTA MEDICINE the competition is being discontinued. The picture editor now invites all physician-photographers to send 35 mm. color slides of suitable subjects for consideration as cover pictures. The format must be horizontal because of printing limitations. Pictures highlighting Minnesota seasons, places, and activities will have an automatic advantage. No limit as to the number of slides sent will be set, but all slides should be individually identified. All slides will be returned. Physicians whose pictures are used as covers will be recognized in MINNESOTA MEDICINE. We can use many more pictures than we have received in the past.

Quackery in the Middle Ages

There are so many little arts used by mountebanks and pretenders to physic, that an entire treatise, had I a mind to write one, would not contain them; but their impudence and daring boldness is equal to the guilt and inward conviction they have of tormenting and putting persons to pain in their last hours, for no reason at all.

Now some of them profess to cure the falling-sickness, and thereupon make an issue of the hinder part of the head, in form of a cross, and pretend to take something out of the opening, which they held all the while in their hands. Others give out, that they can draw snakes or lizards out of their patients' noses, which they seem to perform by putting up a pointed iron probe, with which they wound the nostril, until the blood comes: then they draw out the little artificial animal composed of liver, etc.

Some are confident they can take out the white specks in the eye. Before they apply the instrument to that part, they put in a piece of fine rag into the eye. Some again undertake to suck water out of the ear, which they fill with a tube from their mouth, and hold the other end to the ear; and so spurring the water out of their mouths, pretend it came from the ear. Others pretend to get out worms, which grow in the ear, or roots of the teeth. Others can extract frogs from the under part of the tongue; and by lancing make an incision, into which they clap in a frog, and so take it out.

What shall I say of bones inserted into wounds and ulcers, which, after remaining there for some time, they take out again? Some, when they have taken out a stone from the bladder, persuade their patients, that still there's another left; they do this for this reason, to have it believed, that they have taken out another. Sometimes they probe the bladder, being altogether ignorant and uncertain, whether there be a stone or no. But if they don't find it, they pretend at least to take out one they have in readiness before, and show that to them.

Sometimes they make an incision in the anus for the piles, and by repeating the operation often bring it to a fistula or an ulcer, when there was neither before. Some say they take phlegm, or a substance like unto glass, out of the penis or other part of the body, by the conveyance of a pipe, which they hold with water in their mouths. Some pretend that they can contract and collect all the floating humors of the body to one place by rubbing it with winter cherries; which causes a burning or inflammation; and then they expect to be rewarded, as if they cure the distemper; and after they have supplied the place with oil, the pain presently goes off.

Some make their patients believe they have swallowed glass; so, taking a feather, which they force down the throat, they throw them into a vomiting, which brings up the stuff they themselves had put in with that very feather. Many things of this nature do they get out, which these imposters with great dexterity have put in, tending many times to the endangering the health of their patients, and often ending in the death of them.

Such counterfeits could not pass with discerning men, but that they did not dream of any fallacies, and made no doubt of the skill of those whom they employed; till at last when they suspect, or rather look more narrowly into their operations, the cheat is discovered. Therefore no wise men ought to trust their lives in their hands, nor take any more of their medicines, which have proved so fatal to many.

—Rhazes (850-923)

Idiopathic Hypopara- thyroidism*

Report of a Case

D. P. DANIOLOS, M.D.**
Bismarck, North Dakota

GENERALLY SPEAKING, hypoparathyroidism is an infrequent condition. Particularly since the surgeons have become aware of it as a serious complication following subtotal thyroidectomy, improvements in surgical techniques have lowered the incidence due to injury or accidental removal of the parathyroid gland. Yet even today the majority of cases seen are secondary to surgical trauma.

Idiopathic hypoparathyroidism, however, is an extremely rare primary condition of unknown etiology.

Bronsky *et al.*¹ in 1958 mentioned that in 434,768 patients in Cook County Hospital, there was only one case of idiopathic hypoparathyroidism.

Steinberg and Waldron,² from Queen's General Hospital (New York), reported a case in 1951 and, in reviewing the entire English and foreign literature, were able to accumulate and analyze 52 cases. They emphasized the rarity of this condition, mentioning that in 213,025 admissions to the Queen's General Hospital during a 15-year period, the diagnosis of idiopathic hypoparathyroidism had been established in only one instance.

In 1939 Drake *et al.*³ established the basic criteria for the diagnosis of idiopathic hypoparathyroidism as follows: low serum calcium level; high serum phosphorus level; chronic tetany; absence of x-ray signs of rickets or osteomalacia; absence of renal insufficiency, steatorrhea, chronic diarrhea and alkalosis (conditions which themselves might cause hypocalcemia and tetany).

The etiology of this disease is of course unknown. Only three cases reviewed by Steinberg came to autopsy. In two of them there was no evidence of parathyroid tissue. In the third, all parathyroid parenchyma was found to be completely replaced by fatty tissue.

*Read at the North Dakota Regional Meeting of the American College of Physicians, September 11, 1965.

**Department of Internal Medicine, Quain & Ramstad Clinic, Bismarck, North Dakota.

Case History

Our patient is a male 51 years of age. The case is of unusual interest because the patient had been symptomatic since the age of 14 and untreated up to this time. It is, I believe, the only case reported in the literature to remain symptomatic for 37 years prior to the institution of therapy. A case reported by Steinberg² was symptomatic 31 years prior to diagnosis.

Until the age of 14 this man was a perfectly normal and healthy boy, doing well in school in a small town in South Dakota. At the age of 14 he had his first seizure, diagnosed by a South Dakota physician as grand mal epilepsy. He then had frequent epileptoid seizures described as tonic and clonic convulsions with some foaming from the mouth and tongue biting. During the first year of his illness he was seen and treated repeatedly by several physicians in South Dakota, who all agreed as to the diagnosis of epilepsy. In spite of proper treatment the boy continued having frequent seizures and, in addition, became extremely restless, nervous, and difficult to manage. He was forced to quit school. During this first year of illness he became so disturbed and unmanageable physically as well as mentally and emotionally that he was finally committed to the Jamestown State Hospital where he was treated for approximately two years until he was 16. There he was diagnosed as suffering from epileptic psychosis and mental deterioration.

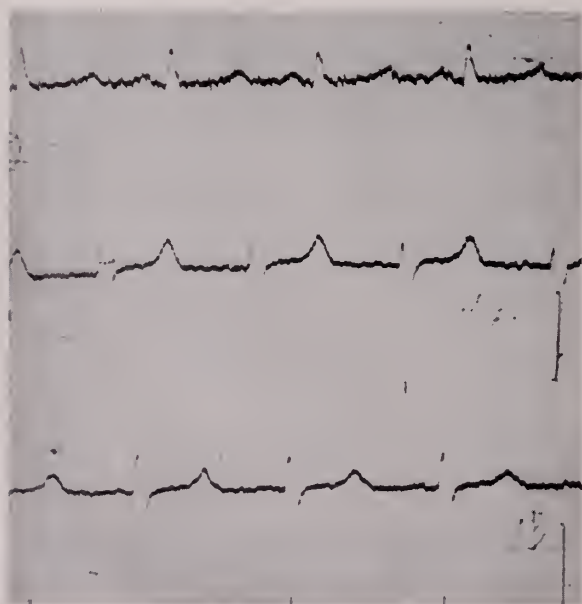
Following his discharge from the state hospital he was maintained on anti-epileptic medications, but continued having convulsions and showing slow, progressive mental deterioration. He lived with his family on the farm and was able to do a few chores around the place until several years ago when he became entirely unable to function mentally or physically at home. Anti-epileptic medications used throughout the course included phenobarbital, mebaral, dilantin and mysoline.

At the age of 22 his vision started failing and two years later he was able to see nothing with the right eye and only very faintly with the left. At that time a diagnosis of bilateral cataracts was made and a mature cataract was extracted from the right eye. A secondary cataract gradually developed over the right eye which had to be operated upon in 1961. The same year a mature cataract was also dissected from the left eye.

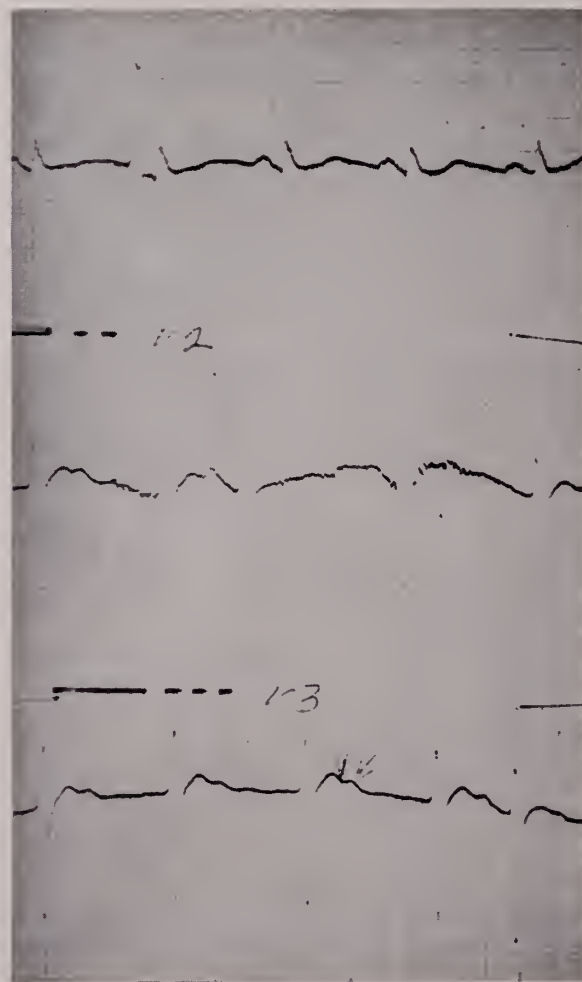
During the last five years this patient has been repeatedly treated at the clinic and in the hospital, mainly because of recurrent severe epileptic seizures and mental retardation.

Physical Findings

In March, 1965, he was admitted to the Bismarck Hospital complaining of severe sore throat, edema of the tongue, and hoarseness of voice. He was treated with various agents for approximately one month with no improvement. A direct laryngoscopy and biopsy were performed which revealed inflammatory laryngitis, nonspecific. The physical examination at that time was essentially unremarkable, except for the local inflammatory changes of the mouth and throat, the residual



Graph 1



Graph 2

IDIOPATHIC HYPOPARATHYROIDISM—DANIOLOS

of the bilateral cataract changes, the evidence of mental retardation, marked irritability and tremor, and a generalized muscular spasticity particularly pronounced over the upper extremities where a typical carpal spasm was noted. A strongly positive Trousseau sign was easily discernible, but Chvostek's sign could not be induced. There was no evidence of hair or skin abnormality, though one of his fingers did show changes suggestive of old mycotic infection.

Laboratory Findings

An electrocardiogram revealed a heart rate of 75, a QT interval of 0.48 seconds and a QTc of 0.5 seconds, a tracing definitely suggestive of hypocalcemia (Graph 1). A serum calcium was reported as 4.5 mg.% with a serum phosphorus of 3.5 mg.%. His voice continued extremely hoarse for several days and he soon developed a typical laryngeal stridor.

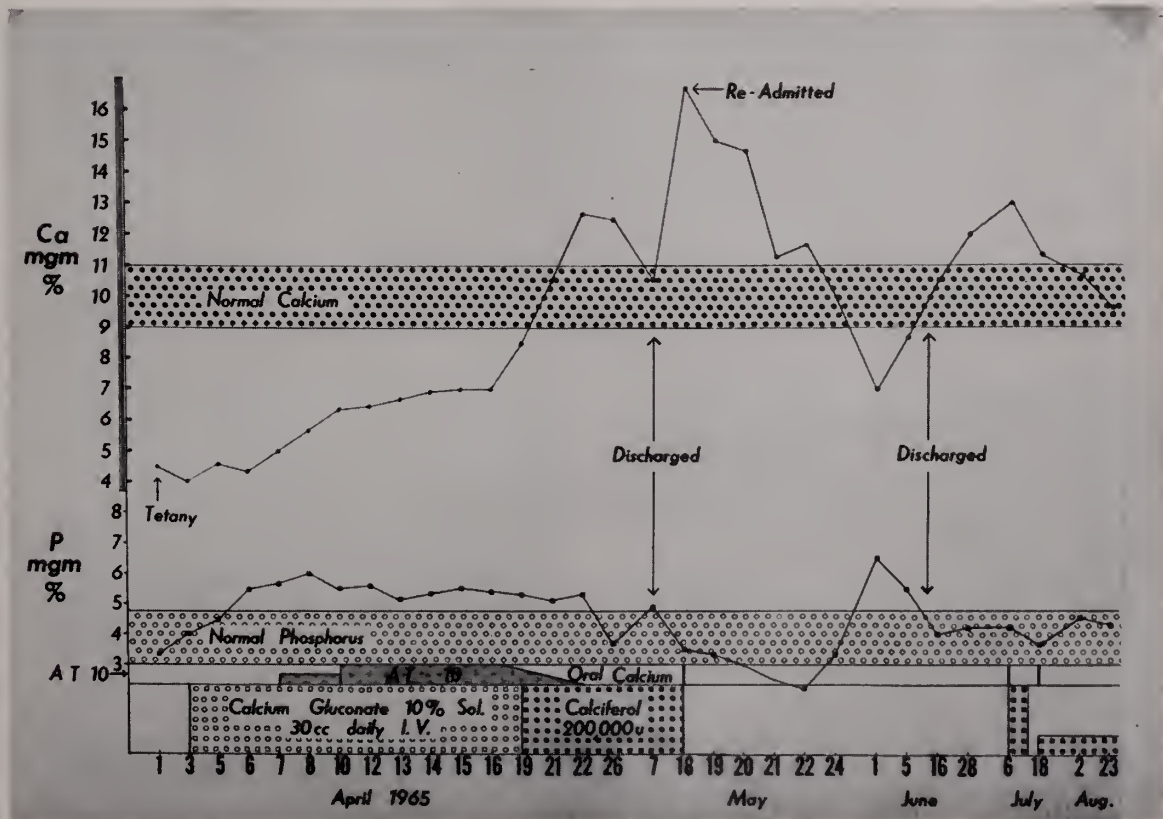
A repeat evaluation of the serum calcium was reported as 4 mg.% with a serum phosphorus of 4.6 mg.%. Laboratory studies including BUN, alkaline phosphatase, urinalysis, fasting blood sugar, serum creatinine, wbc. and differential were all within normal limits. Total proteins were 5.8 grams with a normal A/G ratio. Serum sodium and chlorides were normal, but the serum potassium was low, 3.3 mEq/l. A 24-hour urinary secretion of calcium was 6 mg.% with a normal of 100 to 300 mg.%. X-ray studies of the chest, intravenous pyelogram, stom-

ach and colon were all normal except for a hiatus hernia. A bone x-ray survey revealed no abnormalities except for calcification of the area of the basal ganglia of the brain. An electroencephalogram was within normal limits (this was the first electroencephalogram ever obtained on this patient).

Treatment

He was treated with intravenous calcium gluconate and calcium lactate orally, dihydrotachysterol (AT-10) (later substituted for by calciferol), a low phosphorus diet and supportive care. His improvement was striking. The muscular irritability and spasticity were promptly relieved; the laryngeal stridor and the mouth and throat discomfort disappeared. Confusion and mental attitude were markedly improved, and two weeks after the initiation of therapy he was able to carry on an almost normal conversation. His family commented that his improvement was so striking they could hardly believe it. Throughout this period no anti-epileptic medications were used and the patient had no convulsions.

He was discharged on April 27, 1965, on calcium lactate, vitamin D 500,000 units q.i.d. and a low phosphorus diet. On discharge the serum calcium was 10.4 mg.%; serum phosphorus, 5 mg.%; a 24-hour urinary secretion of calcium, 162 mg.% (normal 100 to 300 mg.%) and a 24-hour urinary excretion of phosphorus, 250 mg.% (with a normal of 900 to 1,300 mg.%).



Graph 3

Overtreatment

On May 18, 1965, the patient was re-admitted to the hospital complaining of persistent and severe constipation, not relieved by strong laxatives. There was associated abdominal distress, marked anorexia and fatigue. Examination revealed him to be markedly dehydrated, confused, and difficult to understand because of thickness in his speech. There was poor oral hygiene, considerable redness and congestion of the throat and excessive thick mucous secretion in his mouth and throat. A fecal impaction was present. An electrocardiogram revealed a rate of 80 with a QT of 0.24 and a QTc of 0.25 seconds indicative of hypercalcemia. There were prominent U waves suggestive also of hypopotassemia (Graph 2). The serum calcium on that date was 16.6 mg.% with a serum phosphorus of 3.9 mg.%; a serum potassium was 2.6 mEq/l. It was obvious that he had been overtreated. After hydration 10 days later his serum calcium had declined to 6.8 mg.%, the phosphorus to 6.6 mg.% and the patient was again placed on vitamin D and calcium lactate. Since then he has been followed regularly at the clinic and has been maintained on a smaller dosage of Calciferol and no calcium. Graph 3 indicates the patient's course during the interval of 4/1/65 to 8/1/65 with the values of serum calcium and phosphorus and the therapy used during that interval. Since then he has been extremely well, entirely free of any convulsive seizures. He is able to care for himself, work on the farm regularly, and though he is not yet the brightest man on earth, he is able to do things that he had never previously done. Figures 1 and 2 are "before and after" photographs, indicating the obvious improvement.

Comments

In spite of the rarity of idiopathic hypoparathyroidism, the physician should be on the alert for its existence, since the serious complications that may occur if the disease remains undiagnosed could lead to tragic results and perma-

nent serious mental and physical deficiency as shown in this case. Certainly of interest is the ease with which the wrong diagnosis made 37 years ago could mislead a large number of physicians who periodically examined and treated this patient. The improvement in physical and mental status shown after accurate therapy was established was indeed striking.

Tetany

The most common symptom of idiopathic hypoparathyroidism is tetany which, according to Steinberg and Waldron², occurs in 78% of cases. Convulsions occur in 52% and less frequently gastrointestinal disturbances, psychosis, photophobia, and blepharospasm.⁶ In spite of the low incidence and questionable connection of psychosis to idiopathic hypoparathyroidism, the observation of psychosis by Green and Swanson⁴ in five cases of hypoparathyroidism following thyroidectomy is of interest. The psychosis in all those cases responded favorably to the therapy of hypoparathyroidism.

Physical Change

Cataracts were found in 50% of the 52 cases analyzed by Steinberg and Waldron.² These may occur very early in life. Other less common signs are teeth, skin, nail and hair changes, papilledema, fungus infections, mental retardation and chronic conjunctivitis.

Calcium and Phosphorus Abnormalities

Laboratory findings with the exception of the



Figure 1



Figure 2

*See Test Your Word Score Page 1097.

calcium and phosphorus abnormalities are essentially unremarkable. Cantarow and Trumper⁵ mention that serum P concentration may be normal or elevated. Hypocalcemia is always present. The alkaline phosphatase is generally normal. In our case anemia and hypopotassemia were noted for which we have no clear-cut explanation unless they were related to malnutrition and the chronicity of the patient's illness, particularly since a low potassium level was noted during both the hypocalcemia and the later hypercalcemia state. Of the 52 cases analyzed by Steinberg and Waldron² the cerebrospinal fluid was examined in 15 and found to be abnormal in six cases.

Skeletal Changes

There are usually normal skeletal roentgenographic findings. Skull x-rays, however, did reveal calcification of the basal ganglia in seven of the cases in the Steinberg and Waldron review. (This is interesting since of the seven cases abnormal cerebrospinal fluid was found in one instance, papilledema in two instances and mental retardation in two.) In our case calcification of the basal ganglia was also reported. The electrocardiogram usually reveals a prolonged QT interval.

Therapy

The therapy of idiopathic hypoparathyroidism, rewarding as it is, also involves risks, as clearly indicated in our case. Hypercalcemia with its serious toxic manifestations may easily occur if one is not careful to evaluate with accuracy over prolonged periods of time the amount and type of medication best adapted to the individual case. Dihydrotachysterol (AT-10) may be preferable to initiate therapy, but it is considerably more expensive than vitamin D, and in most instances it is possible to continue therapy with maintenance dosages of vitamin D alone or in combination with calcium. In any case, the patient should be followed closely at regular intervals for the rest of his life.

Summary

We have presented a case of idiopathic hypoparathyroidism manifesting most of the clinical symptoms and signs of the disease, which yet remained undiagnosed for 37 years, the longest symptomatic case ever reported in the literature.

The rarity of this condition was emphasized.

Brief review of the clinical and laboratory findings was given as well as highlights of its therapy.

References

1. Bronsky, D., et al.: Idiopathic Hypoparathyroidism and Pseudohypoparathyroidism. *Medicine* 37:317, 1958.
2. Steinberg, H. and Waldron, B. R.: Idiopathic Hypoparathyroidism; Analysis of 52 cases. *Medicine* 31:135, 1952.
3. Drake, Trumen G., et al.: Chronic Idiopathic Hypoparathyroidism; Report of Six Cases with Autopsy Findings in One. *Ann Intern Med* 12:1751, 1939.
4. Green, J. A. and Swanson, L. W.: Psychosis in Hypoparathyroidism with Report of Five Cases. *Ann Intern Med* 14:1238, 1941.
5. Cantarow, A. and Trumper, M.: *Clinical Biochemistry*. 6th. edition, page 234.

Derivatively Speaking

—*Malaria* was so-called because it was attributed to bad air (Italian *mala* plus *aria*). The instrumentality of the mosquito was not recognized until later; but the name remained unchanged.

Science

Science is a first-rate piece of furniture for a man's upper chamber, if he has common sense on the ground floor.—Oliver Wendell Holmes

Knotgrass

Knotgrass heals broken joints and is powerful by urine to expel gravel and stone.—Nicholas Culpepper

Candida Albicans Syndrome

Alopecia, paronychia, localized or widespread skin eruptions, and dwarfing have been described in association with *Candida albicans*, a genus of yeast-like fungi that causes human infection. Schultz first reported three cases in 1935; only a few additional cases have been recorded. As a rule the condition is limited to childhood.

The pathologic features have been strikingly constant. Despite the presence of widespread skin eruptions, no fungi are regularly cultured from the skin. The organisms may be cultured from lesions of oral mucous membranes and from stools.

The relation of the fungus to skeletal growth or dwarfing and to the scalp (in causing alopecia and loss of hair pigment) is not understood; these effects may relate to the presence of the fungus in the gastrointestinal tract. The intestinal infection with *C. albicans* is reported to be controlled by the use of thymol or of other antifungal agents.

Durham, Robert H.—*Encyclopedia of Medical Syndrome*
Hoeber Medical Division, Harper and Row, New York

Radiology Residents Hold Research Symposium

On Thursday, May 25, 1967, a Residents' Day Research Symposium was held by the Department of Radiology at the University of Minnesota. Eight Medical Fellow Specialists presented papers describing their research projects. Presenting papers on the scientific program and the titles of their papers were as follows:

Dr. James MacGibbon: "Comparison of Bone Scanning Using Strontium ^{87m} with Radiography in the Diagnosis of Bone Lesions"

Dr. Anton Neese: *Primary Lymphedema*

Dr. Stefan Laxdal: *Evaluation of Cesium ¹³¹ in Myocardial Scanning*

Dr. Gail W. Haut: *Single Breath Bronchography*

Dr. David L. Moore: *Study of Pulmonary Radiation Changes in Rabbits Using Radioisotope Techniques*

Dr. Gerald Telander: *Relationship of Tumor-Size to Tumor-Brain Concentration Ratio as Studied in a Brain Phantom with Rectilinear and Scintillation Camera Methods*

Dr. Stephen Kieffer: *Intrathecal Radiogold (Au ¹⁹⁸) in the Treatment of Spinal Axis Neoplasms*

Dr. Gustave Formanek: *Present Standards of Coronary Flow Measurements and Experience Seen on the Xenon ¹³³ Technique*

General Chairman for the program was Dr. Yosh Maruyama.

Feed by measure and defy the physician.—John Heywood



Editorials

Deficiency of Glucose-6-Phosphate Dehydrogenase

IN THE PAST few years a plethora of papers has attested to the growing interest in and recognition of enzymatic defects in hemolytic disorders. This is exemplified in the interesting report of such a case by Lerner and Doscherholmen.¹

By far the commonest enzyme defect leading to hemolytic disease is glucose-6-phosphate dehydrogenase deficiency. On the basis of the high gene frequency (about 13%) of glucose-6-phosphate dehydrogenase deficiency among American Negroes alone, it is estimated that about 3,000,000 people in the United States carry genes for this disorder. Thus, this deficiency is second only to blood-group (Rh) incompatibility as a potential cause of hemolytic disease. Recent large surveys indicate that this may be a commoner cause of anemia than hitherto recognized. Not only oxidant drugs, but diabetic ketosis, pneumonitis, and viral hepatitis as well, have precipitated hemolysis in patients not receiving drugs.^{2,3}

Altogether, at least 24 human erythrocyte variants of glucose-6-phosphate dehydrogenase have been defined, on the basis of electrophoresis, substrate specificity, Michaelis constants, and so forth. Some of the features that distinguish these variants have been indicated by Lerner and Doscherholmen.¹ Major variants associated with low glucose-6-phosphate dehydrogenase levels may be designated: (1) Negro variant; (2) Mediter-

ranean variant; (3) Greek mild variant; (4) undefined variants (for example, Malayan) and (5) congenital nonspherocytic hemolytic anemia variants.

As illustrated by the case reported,¹ glucose-6-phosphate dehydrogenase deficiency is not restricted to any ethnic group, although the gene frequency in those of north European ancestry is only about 1 in 1,000. Except for one case⁴ of a Japanese patient, congenital nonspherocytic hemolytic anemia due to glucose-6-phosphate dehydrogenase deficiency seems to have been recognized almost exclusively in Caucasians, particularly those of north European ancestry. Congenital nonspherocytic hemolytic anemia is of interest in other respects. Qualitative enzymatic changes seem to be almost unique to each affected family.⁵ A puzzling feature has been that heterozygotes* with this disorder most commonly show entirely normal glucose-6-phosphate dehydrogenase levels. This was true of the patient described by Lerner and Doscherholmen¹ and has been true in our experience with three of four families in which males were affected with congenital nonspherocytic hemolytic anemia due to glucose-6-phosphate dehydrogenase deficiency. This phenomenon has led experienced investigators⁶ to postulate that this deficiency in their patient with congenital nonspherocytic hemolytic anemia represented a new mutation rather than hereditary transmission. Other more plausible explanations are that in a woman heterozygously affected with this disorder, (1)

*See Test Your Word Score Page 1097.

Continued



*"When I couldn't even smell corned beef and cabbage,
I decided it was time for you, Doc."*

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the affected erythrocyte cell line may proliferate less efficiently than the normal cell line, (2) the affected cells may be more rapidly eliminated from the circulating blood, leaving only unaffected erythrocytes in circulation, or (3) that due to uniform embryonic inactivation of the abnormal x chromosome, only normal erythrocytes may be found in the blood. Probably all of these mechanisms contribute to making many heterozygous females indistinguishable from normals.

In the past, some patients with congenital nonspherocytic hemolytic anemia due to glucose-6-phosphate dehydrogenase deficiency have been subjected to splenectomy, and in some of these this therapy was based on the results of osmotic fragility studies. Although splenectomy is "curative" in congenital spherocytosis, it has been of little or no benefit in glucose-6-phosphate dehydrogenase deficiency, and infrequent-

ly of benefit in other hemolytic disorders due to enzyme deficiency. Furthermore, infectious or thromboembolic phenomena which occasionally follow splenectomy may lead to morbidity or death. Osmotic fragility is a nonspecific test, the results of which are usually normal in congenital nonspherocytic hemolytic anemia, but may not be decisive. It would seem, then, that one of the many reliable methods for detection of glucose-6-phosphate dehydrogenase deficiency, which can be done in any hematology laboratory, should be applied in all cases of congenital hemolytic disease wherein any question exists as to the underlying mechanism. If glucose-6-phosphate dehydrogenase deficiency is confirmed, splenectomy should not be performed, transfusions should rarely be administered, and exposure to drugs should be carefully restricted.

Virgil F. Fairbanks, M.D.
Rochester, Minnesota

References

1. Lerner, I., and Doscherholmen, A.: Congenital Nonspherocytic Hemolytic Disease With Erythrocyte Glucose-6-Phosphate Dehydrogenase Deficiency: Report of a Case and Review of the Literature. *Minnesota Med.* 49:1387, 1966.
2. Burka, E. R., Weaver, Z., III, and Marks, P. A.: Clinical Spectrum of Hemolytic Anemia Associated With Glucose-6-Phosphate Dehydrogenase Deficiency. *Ann Intern Med* 64:817, 1966.
3. Boon, W. H.: Viral Hepatitis in G-6-P.D. Deficiency. *Lancet* 1:882, 1966.
4. Tada, K., and Mizuno, H.: Demonstration of Metabolic Anomaly in Congenital Nonspherocytic Hemolytic Anemia and Beneficial Effect of Vitamin B₁₂ Upon It. *Tohoku J Exp Med* 74:18, 1961.
5. Kirkman, H. N.: Genetic Control of Human Enzymes. *Pediat Clin N Amer* 10:299, 1963.
6. Weidtmann, V., and Tönz, O.: Glucose-6-Phosphat-Dehydrogenase-Mangel der Erythrocyten bei drei deutschen Kindern: Nachweis einer frischen Mutation. *Klin Wschr* 44:446, 1966.

Food Allergy

MANY AREAS in the practice of clinical allergy are controversial and this is especially true of problems relating to food allergy. There is no doubt that allergy to foods may be important etiologically in many clinical conditions. The question is how this problem can best be approached from a diagnostic standpoint, since treatment is clear as to removal of the offending foods once a definite diagnosis has been made. Diagnostic tests, in general, are on a shaky scientific foundation. Skin testing for offending foods has been found to be generally unreliable. Elimination diets are sometimes helpful. A carefully taken clinical history is certainly important, but patients often are uncertain

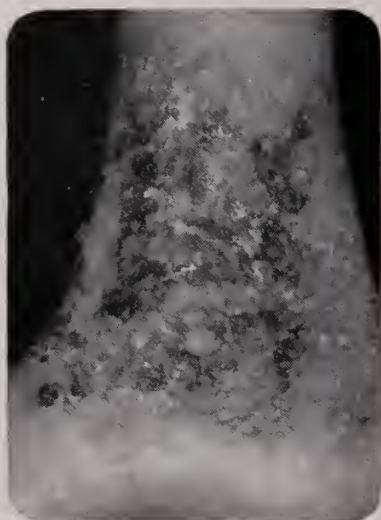
as to the importance of various foods. A provocative diet containing large amounts of the suspected food given on several separate occasions may be a valuable technique. Another type of testing involves the leukopenic index which is based on the unproved idea that leukopenia follows the ingestion of a food to which a patient is allergic.

In the article concerning corn allergy in the present issue, Dr. Johnson* has used the Rinkel technique of giving injections as a test for food allergy and then giving "neutralizing" injections of the same material. This method of diagnosing food allergy has been controversial and the scientific basis is not well established. One cannot deny that Dr. Johnson's patients have benefited

Continued

*Johnson, Kenneth J.: The Importance of Corn Allergy. *Minnesota Med* 50:33, 1967.

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Contraindications: Tuberculosis of the skin, herpes simplex, chicken pox and vaccinia.

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effects are encountered, the drug should be discontinued and appropriate measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive non-permeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyoderma will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

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from his treatment. However, as in most studies in food allergy, controls are lacking. Symptoms which Dr. Johnson described as "throat feeling thicker, something in throat, formation of phlegm in throat, need of clearing of throat, sinus drainage in throat, postnasal drip, runny nose, stuffy nose and throat, dry throat, dry mouth and nose, cough, frothy saliva" may or may not be related to food allergy. The psychologic impact on a

patient of a rigorous program of testing and then elimination of foods is not clear. Judgment in regard to use of the Rinkel technique of diagnosis and treatment of food allergy is not possible because adequately controlled studies have not been carried out.

Harry A. Swedlund, M.D.
Rochester, Minnesota

The Use of Drugs in Mild Hypertension*

ARE ALL OR nearly all hypertensive patients benefited by a pharmacologically-induced normotensive state? This is one of the crucial questions for those interested in hypertension today. It has been established beyond doubt that hypertensive patients have a poorer prognosis for life expectancy than do nonhypertensive patients, and that the severity of the hypertensive disease largely determines the prognosis. There can be little argument about the benefits of antihypertensive therapy in patients with malignant or accelerated hypertension; nor is there much doubt that treatment will improve the prognosis in those patients whose hypertension has produced certain complications in the cardiovascular-renal systems (if renal complications, in particular, are not too far advanced). Mildly hypertensive patients also have a shortened life expectancy, but it remains to be proved conclusively what effect treatment will have on this group of patients. Evidence to date suggests that treatment will be beneficial in preventing or significantly retarding the development of complications that shorten the lives of mildly hypertensive patients, but the hypothesis has not been proved to the complete satisfaction of physicians and others concerned with this problem. The final answer may await results of a carefully controlled, long-term prospective study.

It appears that the beneficial effect of anti-

hypertensive treatment relates to lowering of the systemic blood pressure. Whether this is produced pharmacologically by reducing the peripheral vascular resistance or by reducing cardiac output, whether by interfering with the function of the sympathetic nervous system or by altering sodium metabolism, appears to matter little so long as the systemic blood pressure is reduced.

Were the ideal antihypertensive drug available, one could advocate drug therapy for all hypertensive patients regardless of the severity of the disease. However, all drugs currently in use have potentially harmful effects in addition to the desired antihypertensive actions. In many ways, the thiazide drugs and related agents approach the ideal as antihypertensive drugs. The recent report by Moyer again underscores the applicability of these agents in everyday clinical practice. Yet alteration of carbohydrate metabolism, hyperuricemia, and hypokalemia, which are among the undesired effects, are worrisome, particularly in considering the possible use of these drugs in a patient for 10, 20, or more years. Consequently, the physician who is treating mildly hypertensive patients must weigh carefully the hazards of the disease as they are known against the hazards of drug therapy in his attempt to arrive at the best solution of whether to treat or not to treat.

Philip J. Osmundson, M.D.
Rochester, Minnesota

*Moyer, Richard: Antihypertensive Therapy in Clinical Practice. Minnesota Med 49:1551, 1966.

Optimism

I make the most of all that comes
And the least of all that goes.

Sara Teasdale



"All Interns are Alike"

It stands to reason. They all go through the same training; they all have to pass the same tests; they all have to measure up to the same standards; they all are underpaid, too. Therefore, all interns are alike.

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You might also say that all interns aren't alike, either.



Serious Bleeding During Therapy with Coumarin Compounds

IN THE NOVEMBER issue of MINNESOTA MEDICINE there appears an article entitled "Coumarin Complications" by Reece and Olson.* The authors report eight cases of serious bleeding occurring during therapy with coumarin compounds, with three fatalities. Such a report re-emphasizes the fact that there is risk of serious and possibly fatal hemorrhage when anticoagulant therapy with coumarin compounds is employed. The authors include pertinent comments on the clinical manifestations which may lead to the diagnosis of serious internal hemorrhage in unusual locations.

It seems worthwhile to emphasize the fact that the prothrombin time was well in excess of what is usually considered the upper limit of the therapeutic range in seven of the eight reported cases, when the serious bleeding developed. For a good many years the upper limit of the range of therapeutic hypoprothrombinemia during therapy with coumarin compounds has been considered by most clinicians who have had experience with this type of therapy to be indicated by a one-stage prothrombin time which is two and one half times the normal prothrombin time in seconds. This corresponds roughly in most laboratories to a prothrombin activity which is approximately fifteen per-cent of normal. Many clinicians feel that for long-term therapy the upper limit of the therapeutic range should be even lower, that is, indicated by twice the normal value of the prothrombin time in seconds.

Intravascular thrombosis is a potentially lethal and potentially disabling disease process. There is evidence that it can be prevented or arrested in the majority of cases by adequate anticoagulant therapy. However, after twenty-five years of employment of this method of treatment there is still controversy and disagreement as to just when it should be used. The important thing is for the physician to treat patients and not diseases. Patients should be selected for anticoagulant therapy only after careful consideration of

all facts which might lead to its success or failure.

It has been generally agreed by most experienced clinicians that there are three basic prerequisites for the employment of anticoagulant therapy: an interested and meticulous physician, a patient who is willing and able to follow instructions without deviation, and a reliable laboratory. A primary consideration in the avoidance of serious hemorrhagic complications during anticoagulant therapy is to keep the prothrombin time within the therapeutic range. This requires that determinations of the prothrombin time be done as frequently as is necessary for determining the proper dose of the drug for the individual patient. Maintenance of the prothrombin time within the therapeutic range also requires, as indicated by the authors, particularly close supervision of the patient if there is intercurrent illness, temporary nutritional deficiency, or the employment of other drugs such as salicylates, certain antibiotics and steroids, any of which may augment the action of the coumarin compound.

Most of the severe bleeding complications of coumarin therapy have occurred during periods of excessive hypoprothrombinemia, but it is true that some have occurred when the prothrombin time was within the therapeutic range. Minor but definite bleeding occurring in such patients should always be viewed with suspicion, and serious consideration should be given to discontinuing the anticoagulant therapy. A small group of patients may be encountered whose response to anticoagulants is found to be erratic and fluctuating in spite of frequent prothrombin time determinations and careful attention to dosage. Such patients are rather poor subjects for long-term treatment.

The use of anticoagulants can be a valuable therapeutic tool in the hands of an experienced and careful physician. The indications for its use should be clearly evident. Once treatment is begun it should be continued only if it can be

Continued

*Reece, Richard L., and Olson, Philip A.: Coumarin-Induced Bleeding Complications. *Minnesota Med* 49:1677, 1966.



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closely supervised, and the physician should be prepared to discontinue it immediately if the patient is uncooperative, if the response is erratic, or if hemorrhagic complications develop. If the proper guidelines are followed, it should

be possible to prevent the great majority of serious and fatal hemorrhagic complications.

Nelson W. Barker, M.D.
Rochester, Minnesota

Test Your Word Score

- Amniocentesis** — *aspiration of amniotic fluid from the uterus* (page 1055).
Pernio — *chilblains* (page 1059).
Thrombocytopenia — *abnormally small numbers of platelets in blood* (page 1062).
Plasmacytoma — *a neoplasm composed of plasma cells* (page 1073).
Histiocyte — *one of the elements of the reticulo-endothelial system* (page 1077).
Blepharospasm — *spasm of winking* (page 1086).
Heterozygote — *hybrid* (page 1089).
Ubiquitous — *omnipresent* (page 1103).
Ultracentrifugation — *the process of rapid rotation to separate and sediment the molecules of a substance* (page 1113).
Noncovalent — *without the number of pairs of electrons an atom can share with its neighbors* (page 1117).
Episcleritis — *inflammation of subconjunctival connective tissue* (page 1153).

Chronic Fatigue

In our precious cabbage patches the holometabolous insecta are the hosts of parasitic polyembryonic hymenoptera, upon the prevalence of which rests the psychic and somatic stamina of our fellow-countrymen.

—William Osler

Buckle Up

Smartest thing to wear on your summer vacation is a seat belt. A recent University of Michigan study, financed by the U. S. Public Health Service, indicated the regular use of seat belts by drivers and passengers could have prevented 12,000 traffic deaths in 1965.

Yet last year's annual seat belt survey conducted across the nation during Vehicle Safety-Checks revealed some disturbing figures. Of the 1.7 million cars checked in the survey, more than half were equipped with seat belts. Yet nearly two thirds of the drivers questioned failed to use them when most needed—within 25 miles of the driver's home where four out of five traffic accidents occur.

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Boston Tea Party Relived

Nearly two hundred years ago a minority who were in disfavor of King George III decided to have a party to talk among themselves and let off some steam. Through the ensuing years and down through the pages of history this eminent gathering came to be known as the "Boston Tea Party."

Subsequent to this famous (or notorious) social gathering there arose gross dissatisfaction with the domineering interference by our mother country, and thus was born the American Revolution. History records the fact that we won the war and a free nation was born.

The laws of this free nation are based upon a "Constitution of the United States of America." Within this Constitution was inserted a "Bill of Rights." There have been instances, and there will be still more instances where the laws must be modified or changed for the progress and growth of a great nation.

Now, in our latest law, we are again at the threshold of changes involving the lives of millions of people. We have now formulated and instituted a law giving medical aid to every individual at such time as he attains age 65.

We do not have the fiscal wherewithal to support this program; consequently the "providers of service," as well as the physicians, will be forced to accept fees based upon governmental directives. These fees will be so minimal that the government will then have an excess (on paper only however). At this point a greater number of persons—in categories hitherto not covered—will then become eligible for care. Our individual practices will become completely engulfed in governmental directives.

Like the "Boston Tea Party members," there are only a few of us actively participating to get the law modified—particularly that part which encompasses our welfare recipients.

Unlike the "Boston Tea Party," we will not cause a revolution involving bloodshed. We would like to start an avalanche—an avalanche of letters to governmental officials who have the power to modify or change a law.

Aristotle was correct in his theory when he intimated that the young man was generally too didactic; the middle aged man, who had mellowed and become more pensive with age, had learned to negotiate; and the old man, ready to retire, was complacent in his attitude and willing to accept whatever came his way.

I cannot believe that our peers in the medical profession can be so complacent as to leave as a legacy to those who have so admired them, a record of having done nothing in our great battle for the individual doctor-patient relationship such as they have hitherto enjoyed.

If we must lose this debate with our welfare departments we will have lost one more freedom. Where will it end?

Robert Noreen
Administrator
Broadway-Suburban Clinic
Minneapolis, Minnesota

Bureaucracy: Government of the people, by some of the people and for some of the people.

—*Detroit News*

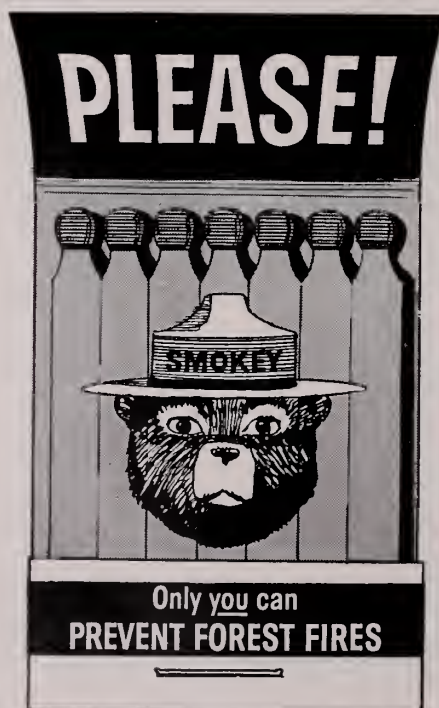


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The Editor's Soliloquy

For Whom Does the Bell Toll?

Living is a physiologic process in which the body is geared to provide its own generator. It has its numerous built-in mechanisms which, under normal circumstances, function well, even when we tax it beyond its normal endurance: a feat impossible for any man-made device.

The dietary inadequacies of three or four generations ago undoubtedly contributed to the smaller stature of our grandparents as compared with the increased stature of the draftees in World War II; but the other privations forced upon those earlier generations no doubt functioned to the advantage of later generation by evolving a better stock through the survival of the fittest.

Now that we have attained this biological pre-eminence, must we corrupt our heritage by over-indulgence in the luxuries our bountiful civilization provides—with its built-in opportunities for indolence and intemperance, as we shift from chaise longue to armchair while sipping our beer, munching our pretzels, and patronizing the most appealing of the carcinogen ads! Instead of being the beneficiaries may we not become the victims of our opulence—with its siren call to self-gratification!

The triple dualities of accidental death via alcoholism, cardiovascular disease via overweight, and cancer via carcinogens, contribute both clinically and statistically the major causes of death in our generation. On the death certificate alcoholism as a contributing factor to accidental death is acceptable; but do overweight or excessive smoking ever appear as accessory causes of cardiovascular disease or lung cancer?

Recently we have been reading about a colony of centenarians in an Aztec tribe in Peru, whose members do not eat, drink, or smoke to excess but live simple lives, maintain regular habits, and engage in daily physical activity. There may be those among us who ask: "Who wants to live that way and who wants to live that long!" But this very question, implying as it does a negative answer, shows how far we have deviated from the wholesome norms of moderation, a virtue fast becoming a casualty of our affluence. Unless we practice more of it, biological regression will be our fate. Nor need we then ask for whom the bell tolls. We shall know!

Carl O. Rice, M.D.

Old Doc Hess says: Some people talk to conceal themselves.

Habit is like a soft bed—easy to get into but hard to get out of.

—Sunshine Magazine

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Curbstone Consultation

Mucormycosis

QUESTION: I referred a patient for thoracic surgery. A left upper lobectomy was performed for bullous emphysema. A copy of the pathologist's report has been sent to me in which it is related that organisms resembling mucormycosis were seen on permanent sections of the lung. What is the significance in the finding of such mucormycosis organisms as described?

ANSWER: In reported human cases *Rhizopus* rather than *Mucor* has been the pathogenic fungus. It is an ubiquitous* organism and is a frequent culture contaminant. As a pathogen it is characterized by its great affinity for spreading to blood vessels. The arteries particularly may become involved, with the formation of a purulent arteritis and thrombosis. It tends to affect specifically diabetics who are poorly controlled. The disease may manifest itself in several forms. The pulmonary form may be primary or hematogenous in origin with thromboses of the pulmonary vessels taking place. As a result, pulmonary infarcts and lobular pneumonia may occur. In the absence of such clinical manifestations in the case described it is not likely that the organisms are pathogenic.

*See Test Your Word Score Page 1097.

Harold D. Kletschka, M.D.
Syracuse, New York

I Chose Medicine

My sister and I decided that we must train ourselves to earn our living, for the family finances were rapidly diminishing and our only hope of a wide and full life, of going out into the big world, lay in our own efforts. There seemed only a few careers open to us—teaching, nursing, the practice of medicine. I chose medicine, not because I was scientifically-minded, for I was deeply ignorant of science. I chose it because as a doctor I would go anywhere I pleased—to far-off lands or to city slums—and be quite sure that I could be of use anywhere.

—Alice Hamilton (1896-) in *Why We Became Doctors*
edited by Noah D. Fabricant, M.D., 1954

Editor's Note: Alice Hamilton specialized in industrial medicine.

In Appreciation

The Minnesota State Medical Association would like to express its appreciation to the firms listed below. These firms were technical exhibitors during the recent 114th Annual Meeting of your Association. Their participation in our annual meeting contributed much to its success.

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The Viewing Box

Traumatic Obstruction of the Duodenum

ON SEPTEMBER 22, 1966, a twenty-nine-year-old white male was driving a truck that struck the rear of a bus. In the accident he was thrown against the steering wheel. The patient presented with rather severe upper abdominal pain, but no nausea or vomiting. He was admitted to the hospital for observation. Admission roentgen study showed a minor degree of localized paralytic ileus involving the upper abdomen. Serum amylase was normal and the hemogram was unremarkable. The patient tolerated liquids and a soft diet very well. He became symptom-free within twenty-four hours and was discharged.

On September 29, 1966, the patient began to experience postprandial episodes of upper abdominal pain associated with a feeling of fullness. On two occasions vomiting occurred. This relieved the feeling of fullness and alleviated the abdominal pain. An upper gastrointestinal barium study was done on October 3, 1966. This examination revealed moderate dilatation of the stomach and proximal duodenum due to partial obstruction in the third and fourth portions of the duodenum (Arrows, Figure 1). There was an irregular constriction of the distal



Figure 1

Continued

THE VIEWING BOX

duodenum with distorted coarsened mucosal pattern (Arrows, Figure 2). The patient was admitted to the hospital and treated conservatively with gradual increase from a liquid to a soft diet. Within five days he became asymptomatic and was discharged.

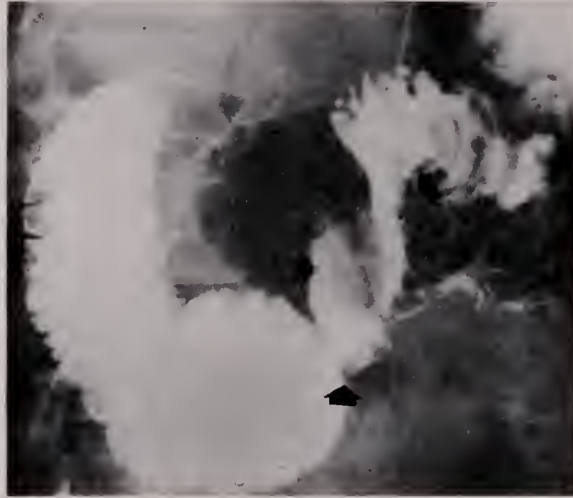


Figure 2

Following discharge from the hospital the patient remained symptom-free. On October 21, 1966, he had a repeat upper gastrointestinal study. This examination showed clearing of the gastric and duodenal dilatation. Only minimal irregularity of the lumen and mucosal pattern remained in that portion of the duodenum which had shown constriction and a stretched mucosal pattern (Arrows, Figure 3).

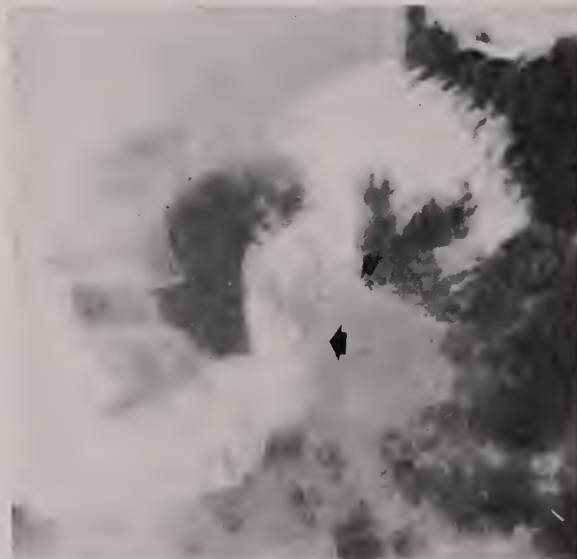


Figure 3

The patient has remained asymptomatic to the present time. He was scheduled for another gastrointestinal study the latter part of March, 1967. What is your diagnosis? (See next page.)

Diagnosis: Intramural duodenal hematoma

The clinical course and radiographic findings in this case are consistent with a diagnosis of intramural duodenal hematoma. Trauma to the duodenum resulting in intramural hematoma is being recognized and reported with increasing frequency. The classic insult is forceful impact against a steering wheel; however, even light blows may cause injury. The postbulbar portion of the duodenum is retroperitoneal and is firmly attached to surrounding structures. It has points of acute angulation and often a fluid content, factors which make the duodenum vulnerable to blunt trauma with compression against the vertebral column.

Intramural hematomas may involve the duodenum from below the ampulla of Vater to the ligament of Treitz and may even involve the proximal jejunum. The total involvement is usually ten to twenty centimeters in length. In cases where duodenal resection was deemed necessary, the surgical specimen showed an edematous, hemorrhagic serosal surface with severe distortion of the muscularis by hemorrhage.

Symptoms following trauma may be immediate; however, there is commonly a latent period of days or weeks between the time of trauma and the clinical and roentgenological manifestations. The chief symptoms are upper abdominal pain of varying severity and vomiting episodes which become more frequent. The history of blunt trauma to the abdomen and this symptomatology are prime indications for plain film study of the abdomen and especially gastrointestinal contrast study. This examination is diagnostic of obstruction. The specific nature of the obstruction can often be suggested.

The radiographic findings typically show varying degrees of gastric and duodenal dilatation proximal to the site of obstruction. The obstruction may be partial, which is the usual situation, or rarely complete. At the site of the intramural hematoma, one of two appearances may be noted: The first of these is the irregular constriction of the lumen with associated widening and irregularity of the mucosal folds; the other is the typical coiled spring stretching due to flattening of the valvulae conniventes by the hematoma.

Other causes of intramural duodenal hematoma besides trauma are pancreatitis, carcinoma of the pancreas, and bleeding diatheses such as hemophilia and anti-coagulant therapy. One other cause recently reported is an iatrogenically-produced intramural duodenal hematoma due to a per-oral small-bowel biopsy with a Ross biopsy capsule.

Consideration must also be given to the occurrence of associated trauma to other organs. Approximately fifty per cent of the cases of intramural duodenal hematoma are associated with some degree of trauma to the pancreas. Fractures of solid viscera such as the liver, spleen, and kidneys may occur. Out-right rupture of the duodenum may also occur, usually at the junction of the second and third portions. Air and blood from the site of the rupture may pass either retroperitoneally or intraperitoneally. Occurrence of associated injury to other intra-abdominal organs obviously compounds the difficulties of diagnosis.

Sewell S. Gordon, M.D.*
Donald C. Hauser, M.D.*
St. Louis Park, Minnesota

*Department of Radiology, St. Louis Park Medical Center.

References may be secured from the author or the reprints.

Address for reprints: St. Louis Park Medical Center, 4959 Excelsior Boulevard, Minneapolis, Minnesota, 55416.

Venereal Disease A Serious National Problem, Says AMA

Venereal disease is spreading so rapidly that it now represents this nation's most urgent communicable disease problem.

VD is hitting particularly hard among teenagers and young adults, according to the American Medical Association.

The venereal diseases are infecting about two Americans a minute—3,000 a day, or 1,100,000 a year. Cases of infectious syphilis have almost tripled in this country in the past five years. More than a million

new cases of gonorrhea are developing annually.

VD can blind, cripple, and even kill.

The ravages of venereal diseases are all needless tragedy, says the AMA, because both syphilis and gonorrhea can be avoided. If contracted, they can be cured by prompt medical treatment.

The cure for both diseases—penicillin—has been available since 1943. Any family physician or public health clinic can administer

prompt treatment.

Venereal disease is caused by intimate personal contact.

Complacency, ignorance, and a free-and-easy attitude toward moral standards are partly responsible for the spread of VD; the increasing use of alcohol, especially among young people, also plays a role.

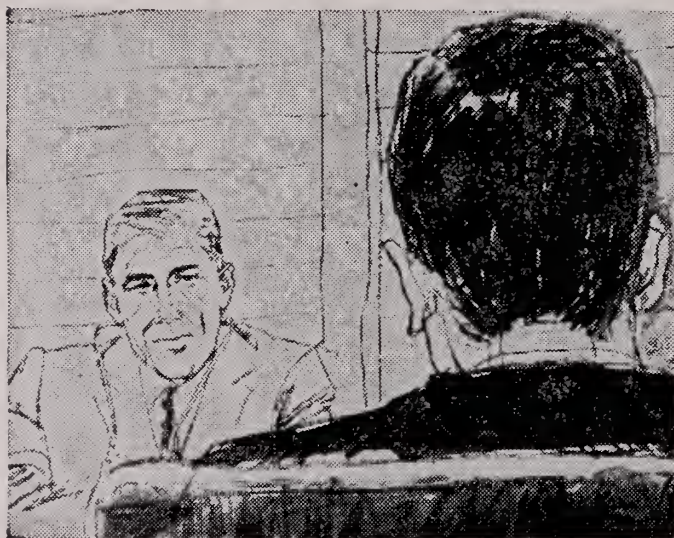
Authorities believe, however, that thousands of young people simply aren't aware of the dangers of VD. Once infected, they are complacent about treatment.

One of the first signs of syphilis may be a painless, ulcerating sore. Gonorrhea produces inflammation of the genital and urinary tracts, and a discharge of pus.

A person may contract syphilis and be unaware that he has the disease. After the first symptoms, the germs may remain hidden in the body for as long as 20 years before any damage is discovered. Then the person may become crippled, develop heart disease, blood vessel disease, blindness, or show mental symptoms. Even death may result from this hidden stage of syphilis.

If left untreated, gonorrhea may be responsible for arthritis, endocarditis, sterility, and blindness.

If a person suspects he may have contracted venereal disease, he should go to a physician immediately.



VD should be treated promptly by a physician.

Tumor Conference

Mucocele of the Appendix and Jelly-Belly (Pseudomyxoma Peritonei)

MUCOCELE OF the appendix is not regarded as a true neoplasm. It is usually considered a cystic dilatation of the terminal appendix due to cicatricial obstruction of the proximal appendix. The thin-walled mucocele is generally filled with thick mucus. The mucous membrane has usually been replaced by a single layer of mucus-producing cells or glands similar to those found in the colon. Rupture of a mucocele and spillage of its contents may result in the spread and growth of mucus-secreting cells over the peritoneal surfaces with the secondary accumulation of gelatinous mucus in the peritoneal cavity (pseudomyxoma peritonei). There is no agreement as to whether pseudomyxoma peritonei is only a non-neoplastic proliferation of mucosal cells stimulated by irritation or a true neoplastic epithelial proliferation.

Neither mucocele nor pseudomyxoma peritonei is common. Incidence is reported as follows^{1,2,5}: (a) 2 to 4% of all appendiceal tumors are mucocèles; (b) appendiceal tumors are found in 0.3 to 1% of all removed appendices; (c) appendiceal tumors constitute 0.1% to 0.2% of all intestinal neoplasms. Since mucocele of the appendix is a rare entity, a recent case prompted us to review the experience with mucocèles (and the even rarer cases of pseudomyxoma peritonei) at the Minneapolis Veterans Administration Hospital.

This case of a mucocele illustrates the frequent presenting complaint of a right lower quadrant mass in an otherwise asymptomatic patient.

Case Reports

Case I

A 40-year-old man, whose private physician found a palpable, round, nonfixed mass measuring 5 cm. in diameter in the right lower quadrant of his abdomen on routine examination in April 1964, refused to have the recommended surgery at that time. The patient's only symptoms were fullness and tightness in his right lower abdomen. Two barium enemas, one in April 1964 and a second in October 1964, did not show any abnormality of the colon. The patient continued symptom-free and was followed by his physician at six-month intervals. The mass persisted.

Laboratory and X-ray Findings

The patient was admitted to the hospital in July 1966. All laboratory work was within normal limits: hemoglobin, leukocyte count, prothrombin time, blood urea nitrogen, fasting blood sugar, serum proteins, alkaline phosphatase, sugar glucose tolerance, bilirubin, serum electrolytes and multiple stools for occult blood. On lumbosacral spine films a calcific

Continued

TUMOR CONFERENCE

density was seen lateral to the spine at the level of L5-S1 (Figure 1). A barium enema showed an irregularity of the posterolateral wall of the cecum, suggestive of adenoma or a carcinoma (Figure 2). A chest film, an intravenous pyelogram, and an electrocardiogram were normal.



Fig. 1 — This abdominal film shows the unusual calcification overlying the iliac bone. The calcification was in the area of the palpable mass.



Fig. 2 — A barium enema shows the deformity of the cecum.

Operative Findings

At surgical exploration in December 1966, a 10 x 6 x 6 cm. mass was found in the right lower quadrant, arising from the appendix and adherent to the cecum and psoas muscle. The tumor was excised widely with 15 cm. of cecum and right colon and 8 cm. of ileum. Continuity was restored with an iliotransverse colostomy. Sections through the proximal appendix, cecum and ileum were normal. Sections through the lesion in the distal retrocecal appendix showed fibrous walls lined by simple columnar epithelium. The mucous material contained rare clumps of morphologically, benign columnar cells. After an uneventful post-operative course, the patient is currently being followed in our Out Patient Department. He has probably been cured.

Since 1941 seven mucocèles of the appendix and three cases of pseudomyxoma peritonei have been seen at the Minneapolis Veterans Administration Hospital. All the patients were men between 28 and 74 years old. Of the seven mucocèles, one unusual case was associated with a proximal carcinoid. Two cases were found incidentally at autopsy; another was found incidentally during a gastrectomy for duodenal ulcer disease. Only one presented with the symptoms and signs of an acute appendicitis. The remaining two patients were operated on because of palpable right lower quadrant abdominal masses. None of the seven mucocèles had ruptured. The five patients, whose diagnosis was made during life, have been seen at the Minneapolis Veterans Administration Hospital in follow-up clinic and are free of recurrent disease for one month in the most recent case to twelve years for the longest follow-up. This curative result for the unruptured mucocèle of the appendix has been found in other series^{1,3,4}.

One group,⁴ studying 136 mucocèles of the appendix with benign epithelium, found no cases of pseudomyxoma peritonei despite an occasional spillage of the

MUCOCELE OF THE APPENDIX

mucocoele contents. Pseudomyxoma peritonei arose secondarily only from those mucocoeles which had been found to contain "Grade I" adenocarcinoma.

The good results of benign mucocoele are contrasted with the unfortunate course of pseudomyxoma peritonei. One brief case history of a typical pseudomyxoma shows some of the problems encountered.

Case 2

A 72-year-old white man had an appendectomy in 1941 at another hospital. Following the operation he was informed that the appendix had contained a "malignant tumor." He was seen postoperatively at regular intervals with no evidence of recurrence until 1964. At that time he noticed gradual abdominal distention, but no other symptoms. He was first seen at our hospital in July 1966. At laparotomy on July 15 the peritoneal cavity was filled with 12,000 cc. of gelatinous material along with many peritoneal implants (Figure 3). After evacuation of the gelatinous material 30 mgm. of nitrogen mustard were instilled intraperitoneally. A month later another 1,500 cc. of gelatinous material was removed by paracentesis followed by intraperitoneal instillation of 22 mgm. nitrogen mustard. The patient's condition deteriorated rapidly and he expired on September 24, 1966. Death was thought to be due to the advanced stage of the disease rather than to the nitrogen mustard administration. The long period (25 years) between the appendectomy and his final episode is certainly noteworthy. It would raise the question as to whether the appendix was the site of origin in this case.

The course of the other two patients with pseudomyxoma peritonei were as fol-



Fig. 3 — This picture taken at surgery shows the many peritoneal implants seen after evacuating the abdomen.

Continued

TUMOR CONFERENCE

lows: One man, 73 years of age, was well until six months prior to admission. His disease progressed rapidly and at the time of admission far-advanced disease prevented anything except supportive, terminal care. The third patient with pseudomyxoma peritonei was found to have his disease during a routine inguinal herniorrhaphy. A subsequent laparotomy showed a ruptured mucocele of the appendix for which a cecectomy was done. At the present time, 3½ years later, there has been no recurrence.

The spectrum of pseudomyxoma peritonei at the favorable end shows a process in which there is leakage of cell-free mucus into the peritoneal cavity from a benign mucocele. If the mucocele is excised, the condition usually regresses spontaneously.^{1,3,4,5} On the other end of the spectrum is the mucocele with an epithelium consisting of malignant cells. This type spills mucus-containing malignant cells which implant themselves on the peritoneal surface and abdominal organs and continue to grow regardless of whether the primary site of origin is removed. Wide excision of the appendix proves curative in the first type, while in the latter, more radical surgery like omentectomy, cecectomy, colectomy, oophorectomy and peritoneal irrigations with nitrogen mustard have only rarely produced long-term survival^{2,4}.

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References

1. Woodruff, R., McDonald, J. R.: Benign and Malignant Cystic Tumors of the Appendix. *Surg Gynec Obstet* 71:750, 1940.
2. Pack, G., Ariel, I.: Treatment of Cancer and Allied Diseases. Vol. 5 Tumors of the Gastrointestinal Tract, Pancreas, Biliary System, and Liver. Paul B. Hoeber, Inc., Med. Division of Harper & Brothers, New York, 1962.
3. Bernhardt H., Young, J. M.: Mucocele and Pseudomyxoma Peritonei of Appendiceal Origin (Clinicopathological Aspects). *Amer J Surg* 109:235, 1965.
4. Byron, R. Jr., Yonemoto, R. H., King, R. M., Lamb, E. J., Ammett, G. D., Solomon, R. D., and Gildenhora, V. B.: The Management of Pseudomyxoma Peritonei Secondary to Ruptured Mucocele of the Appendix. *Surg Gynec Obstet* 122: 509, 1966.
5. Carlton, C.: Mucoceles of the Appendix and Peritoneal Pseudomyxoma. *Arch Path* 60: 31, 1955

For Pain in the Eye (Sixteenth Century)

Take the right eye of a Frogg, lap it in a piece of Russet cloth and hang it about the neck; it cureth the right eye if it be enflamed or bleared. And if the left eye be greved, do the like by the left eye of the said Frogg.*

The Dial Press, New York, 1952, p. 93.

*Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine.

The Sixth Sense

If there is a sixth sense, it is intuition, that instinctive summing up of memories and other evidences collected by the special senses and correlated in man's consciousness.

—William Mayo

Medical Seminar

The Immunoglobulins

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CONSIDERABLE PROGRESS has been made recently in the characterization of the chemical structure and function of antibodies. With this rapid progress has come a certain amount of confusion, in part as a result of varying terminology. The terms (Table 1) recommended by the World Health Organization Committee on Nomenclature of Human Immunoglobulins¹ will be used throughout this review.

Historical Aspects

The acquisition of knowledge about the immunoglobulins has depended on specific technical achievements which opened new avenues of investigation. Among the more important of these technical developments are electrophoresis, ultracentrifugation,* immunodiffusion, and immunoelectrophoresis.

Electrophoresis

Proteins migrate in an electric field at a rate largely dependent on the surface charge of their molecules. Since proteins differ markedly in their net molecular charges, they differ also in their "electric field" mobility at any given pH value. In 1937 Tiselius employed these principles in developing his technique of moving-boundary electrophoresis. By such a technique it was shown that serum proteins could be divided into five fractions: albumin, and α_1 -, α_2 -, β -, and γ -globulins. Shortly thereafter, Tiselius and Kabat² immunized animals and observed an increase in the γ -globulin peak concomitant with increasing antibody titers. When the antibodies were precipitated from the serum by their specific antigens, the γ -globulin concentrations returned to

preimmunization levels. Thus it was shown that humoral antibodies were located in the γ -globulin fraction.

Ultracentrifugation

In 1926 Svedberg and collaborators devised an instrument for obtaining centrifugal fields of sufficient intensity to cause separation of large molecules in solution. Heterogeneous protein solutions could thus be separated on a basis of the different sedimentation rates of the various proteins; the sedimentation rates depend on the size, shape, and density of the molecules. The technique of ultracentrifugation was combined with electrophoresis in studying the γ -globulins by Deutsch and co-workers³ in 1946. Two main components with different molecular sizes and sedimentation coefficients were identified within the γ -globulin family. Small molecules (7S) comprised the larger fraction; the remainder was composed of 19S macromolecules.

Immunodiffusion

In 1946 the technique of immunodiffusion, first used by German workers in 1905 and then discarded, was revived and perfected. The impact of this technique on the developing sciences of immunology and immunochemistry cannot be

TABLE 1
Nomenclature of Human Immunoglobulins

Previous Terminology	Current Terminology
γ_1 7S γ_1 , 6.6S γ_1 , γ_2 , γ_{ss}	IgG or γ G
β_2 A, γ_1 A	IgA or γ A
β_2 M, γ_1 M, 19S γ , γ -macroglobulin	IgM or γ M

*See Test Your Word Score Page 1097.

Continued

overemphasized. Before this time, in-vitro methods of detecting reactions between soluble antigen and its specific antibody consisted of the demonstration of precipitation or flocculation in a fluid medium. Unfortunately, the antigens used were frequently impure; and the flocculate, or precipitate, being examined often consisted of a mixture of many antigen-antibody complexes. Prior to the revival of immunodiffusion techniques, there was no simple method available to detect such impurities or contaminants. The technique of immunodiffusion is simple and extremely sensitive. In brief, antigen is permitted to react with antibody in a gel medium in which each substance diffuses at a rate determined by its concentration and its own specific diffusion coefficient. A line of precipitate forms when an antigen encounters its antibody; this line becomes most pronounced and fixed at the specific location in the gel where equivalence occurs—that is, at the point where the reacting antigen and antibody reach proportions optimal for precipitation. Because of differences in diffusion rates, complex antigen-antibody systems can be resolved in precipitin lines that are distinctly

separated.

Oudin⁴ described a method of test-tube immunodiffusion in 1947. Antiserum was mixed with a warm solution of agar, and the agar was allowed to solidify in a test tube. Antigen solution was then layered on top of the gel and allowed to diffuse into the gelled agar containing the antibody.

Ouchterlony⁵ introduced the important concept of comparative immunodiffusion. In his method, wells are cut in an agar plate equidistant from a central well. Antigen is placed in the outer wells, and the central well is filled with antiserum. The antigen and antibody diffuse into the agar and, on meeting, form a line of precipitation. Ouchterlony noted three principal types of reaction, depending on the relationships between the antigens and antisera used. If the antigens in neighboring wells are identical, the precipitin lines fuse at their contiguous ends; this is termed "reaction of identity" (Figure 1-a). If neighboring wells contain unrelated antigens and the central well is filled with antisera against both, the precipitin lines cross in a "reaction of nonidentity" (Figure 1-b). The final pattern has been

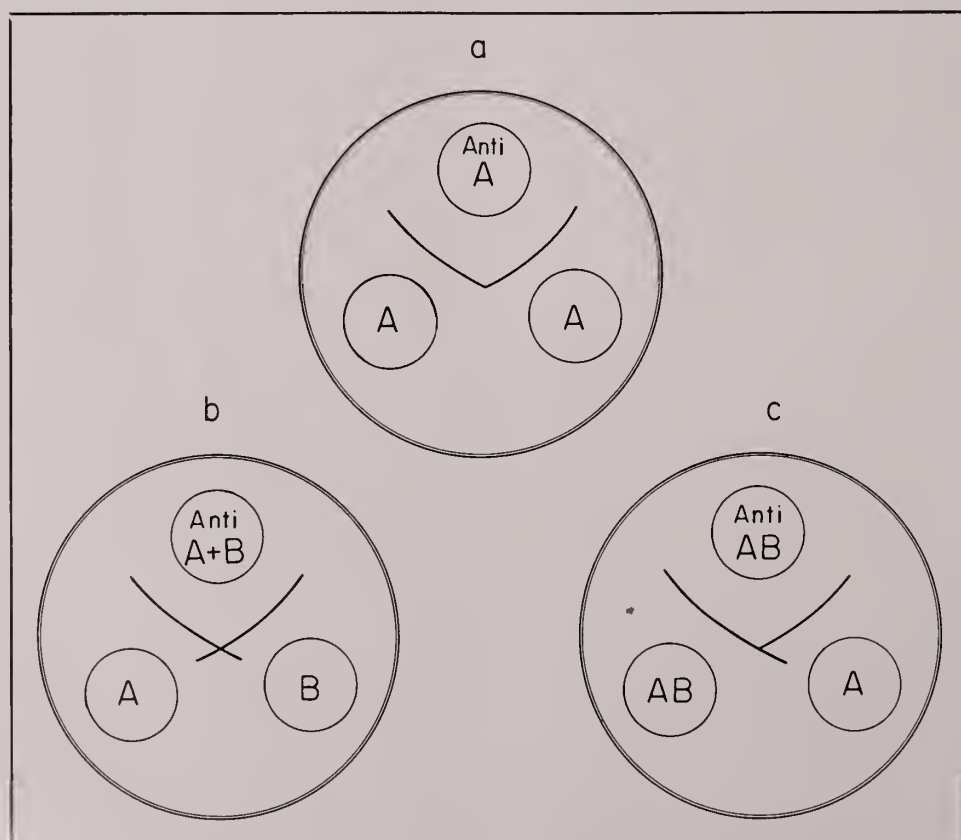


Fig. 1 — Diagram of precipitin patterns obtained by Ouchterlony immunodiffusion technique. (a) Reaction of identity. (b) Reaction of nonidentity. (c) Reaction of partial identity.

termed "reaction of partial identity" (Figure 1-c) and occurs when an antiserum to a complex antigen reacts with neighboring wells, one of which contains the complex antigen, while the other contains a component of but not the complete antigen. Under these circumstances, fusion occurs between the precipitin lines of the identical subfractions; the nonidentical fraction fails to fuse and instead forms a spur from the point of fusion. From study of precipitin patterns on Ouchterlony plates, one can deduce the various types of relationships in complex antigen-antibody mixtures.

Immunoelectrophoresis

In 1953 Grabar and Williams⁶ incorporated the principles of electrophoresis and immunodiffusion into the very important technique of immunoelectrophoresis. Electrophoretic migration is performed in agar gel; immunodiffusion is then accomplished by adding antiserum to a trough cut in the gel alongside and parallel to the field of electrophoretic migration. A series of precipitin lines form as the separated serum protein fractions, diffusing in a radial manner, make contact with the linear margin of the immune serum advancing from the trough. The position of these precipitin lines is determined by the electrophoretic mobility, rate of diffusion, and serologic specificity of each of the proteins present. The technique of immunoelectrophore-

sis can be further manipulated to advantage by using more refined antiserum; for example, specific anti-albumin serum will form a precipitin line only with albumin, anti-transferrin will react only with transferrin, and purified anti- γ -globulin will react only with the γ -globulin fractions of the serum being studied.

Immunoglobulin Subclasses

With the use of these techniques, the complexity of the antibody-containing serum fraction could be studied. It was found on immunoelectrophoresis that this fraction consists of three major groups of proteins now known as IgG (γ G), IgA (γ A) and IgM (γ M) (Figure 2). The IgG fraction is the largest (70%) and has the widest range of electrophoretic mobility, extending from the γ to the α_2 region. IgA (21%) and IgM (7%) migrate in the β - γ area. Two other subclasses have recently been identified in minute quantities in normal human serum and have been named IgD and IgE. Thus the term " γ -globulin" is obviously no longer adequate for this complex mixture of proteins. The more appropriate designation "immunoglobulins" has gained wide acceptance and was recommended by the WHO Committee on Nomenclature.¹ By definition, the immunoglobulins include all proteins with antibody activity plus certain proteins related to them by chemical and antigenic speci-

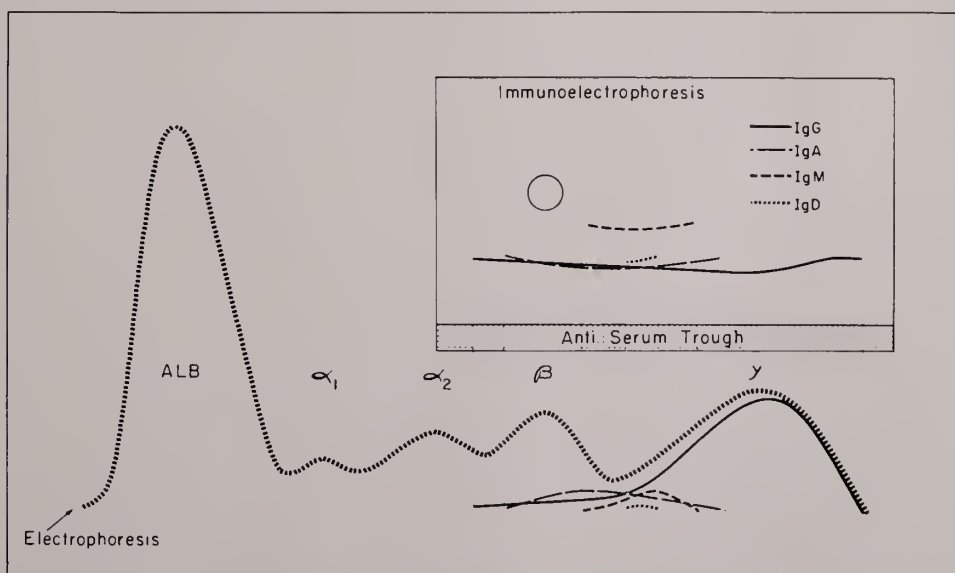


Fig. 2 — Diagram of distribution of immunoglobulins in normal human serum after electrophoresis and after immunoelectrophoresis (Inset). Lines are projected from the immunoelectrophoresis onto the electrophoretic pattern. The areas under these lines indicate the relative amounts and electrophoretic distributions of IgG, IgA, IgM, and IgD.

Continued

ficity. Related proteins, for which antibody activity has not been demonstrated, include the myeloma proteins, Bence Jones proteins, and naturally occurring subunits of the immunoglobulins.

The various subclasses of the immunoglobulins can be isolated from serum by involved physicochemical procedures which include precipitation by organic and inorganic agents, preparative electrophoresis and ultracentrifugation, ion-exchange column chromatography, and gel filtration.

The known properties of these various subclasses are listed in Table 2. Certain specific functions have now been identified for most of the immunoglobulin subclasses.^{7,8}

IgG

This subclass contains many of the recognized antibodies, both to bacteria and to viruses, as well as the factor responsible for the lupus-erythematosus cell phenomenon. All IgG antibodies are actively transported across the placenta.

IgA

The IgA immunoglobulins include antibodies against insulin in persons with diabetes and against thyroglobulin in persons with thyroiditis; however, these antibodies have also been identified in the IgG and IgM subclasses. Antibodies against ragweed and *Brucella abortus* are also of the IgA variety. A special form of these globulins is present in secretions (saliva, colostrum, and bronchial secretions).⁹ More than 90% of the immunoglobulin in secretions is of the IgA variety as opposed to 21% in the serum.¹⁰ The secretion IgA differs from the serum IgA in having an additional piece on its molecule; the function of this moiety has not been determined.

IgM

Immunoglobulins formed in the newborn belong almost exclusively to the IgM subclass. In later life, IgM immunoglobulins are usually the first antibodies to appear after antigenic stimulation and are rarely associated with immunologic

TABLE 2
Properties of Immunoglobulins

Property	Subclass			
	IgG	IgA	IgM	IgD
Amount	75%	21%	7%	0.2%
Mol. wt.	150,000	>150,000	900,000	?
Ultracent.	6.6S	6.6, 9, 11, & 13S	19S	7S
Electrophoresis	γ to α_2	Slow β	Between β & γ	Between β & γ
Carbohydrate	2.5%	10%	10%	?
Average serum level (gm/100 ml.)	1.24	0.39	0.12	0.003

TABLE 3
Immunoglobulin Deficiency States

State	IgG	IgA	IgM
Lymphoid aplasia (Swiss type agammaglobulinemia)	A	A	A
Sex-linked congenital agammaglobulinemia (Bruton type agammaglobulinemia)	A	A	A
Ataxia telangiectasia	N	A	N
Selective IgG, IgA deficiency	A	A	N
Selective IgA, IgM deficiency	N	A	A
Selective IgA deficiency	N	A	N

A = absent; N = normal.

memory. The IgM subclass contains the isohemagglutinins, cold agglutinins, rheumatoid factor, antibodies against somatic O antigens of gram-negative bacteria, heterophil antibodies, and Wassermann antibodies.

IgD

This subclass was recently identified by Rowe and Fahey¹¹ in a patient with a myeloma protein that did not react with known myeloma antisera (anti-IgG, anti-IgA, or anti-IgM). Antiserum was prepared for this unique protein and tested against normal human sera; it was found that normal human serum contains minute quantities of these antigenically distinct immunoglobulins which have been named IgD.¹² Studies are now in progress to determine the immunologic function of the IgD immunoglobulins.

IgE

Quite recently, another subclass was described¹³ and tentatively named IgE. It apparently contains reagin activity previously thought to be associated with the IgA fraction.

Structure of the Immunoglobulin Molecule

The immunoglobulin molecule is a complex

*See Test Your Word Score Page 1097.

composite of structural and functional subunits.^{8,14,15} Many subunits have been identified, but their exact intramolecular positions and associations have not been determined with certainty. From available experimental information there is strong evidence that human IgG consists of four polypeptide chains (two light chains with molecular weights of about 20,000 and two heavy chains with molecular weights of approximately 52,000) held together by interchain disulfide bonds and noncovalent* interactions (Figure 3). It is surmised that each light chain is linked to a heavy chain by a disulfide bond and a third disulfide bond connects the two heavy chains. These disulfide bonds can be disrupted by reducing agents such as mercaptoethanol, thereby liberating the individual light and heavy chains. It is generally assumed that the participation of light and heavy chains in the structure of IgA conforms to that of IgG with the exception of the tendency of the IgA subclass to form polymers. It has recently been concluded that, at least in rabbits, IgM molecules are composites of five monomers, each having the "two light chain and two heavy chain" configuration. However, the heavy chains of IgM appear to be larger, with molecular weights in the range of 70,000.¹⁶

Each individual immunoglobulin molecule is symmetric, the participating light chains and

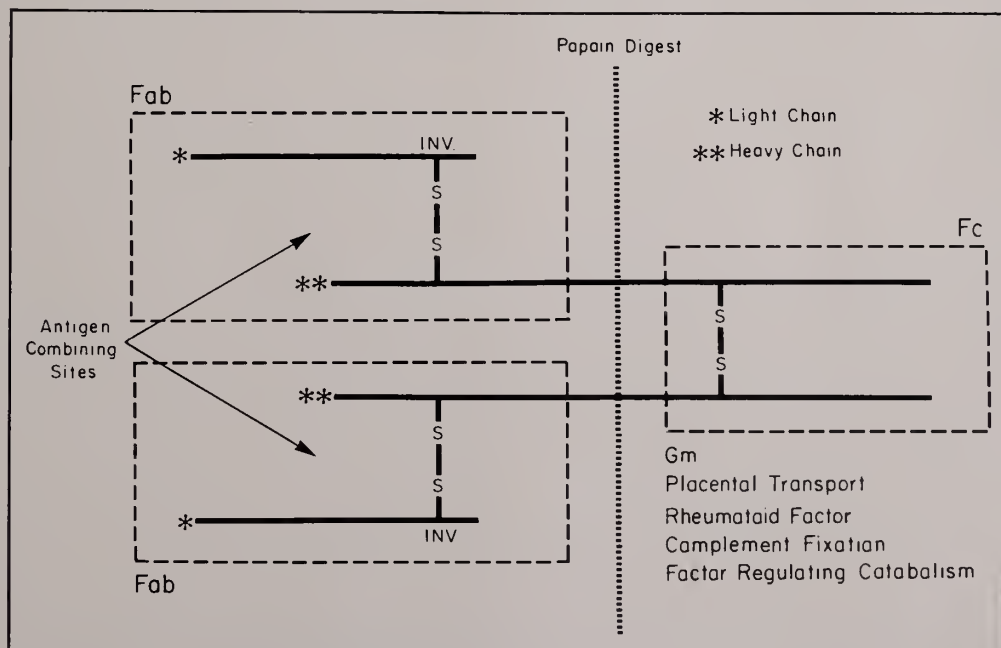


Fig. 3 — Porter model for IgG molecule. List in lower right shows known active sites on Fc fragment (see text).

Continued

heavy chains being identical. Dissimilarity of polypeptide chains has not been discovered within the molecule in nature although hybrid molecules have been synthesized *in vitro*. The light chains must be associated with a particular part of the heavy chains for the full expression of antibody-combining activity. Although not known for certain, it is thought that the carbohydrate component of the immunoglobulin molecule is associated with the heavy chains.

Light chains are of two antigenic types—type K and type L—which are common to all immunoglobulin subclasses and occur with a frequency of 70% for type K and 30% for type L. The light chains of the immunoglobulin molecule are indistinguishable from the Bence Jones proteins that occur in many patients with plasmacytic myeloma. The heavy chains are specific for each subclass; therefore they determine whether the molecule belongs to IgG, IgA, IgM, and so forth. It is also the heavy chains that confer on a particular immunoglobulin molecule its unique antibody specificity.

Further information relating structure to function was gained by studying the effects of the enzyme papain on the IgG immunoglobulin molecule. It was found that papain splits peptide bonds in the two heavy chains, releasing three fragments, one Fc and two identical Fab fragments (Figure 3). The Fab fragments were so named because each contains an active antibody combining-site formed by a light chain in association with a specific portion of the heavy chain. In addition, the Fab fragments have a specific genetic marker termed InV located on the light chains. On the Fc fragment—so named because this fragment is crystallizable—are located such functional groups as the site for complement fixation, the site for rheumatoid factor activity, and a factor regulating catabolism. Apparently IgG passes the placental barrier because of the presence of an active transport site on the Fc portion of its molecule; no such site is present in the IgA or IgM molecules. The Fc fragment also contains a genetic marker termed Gm.

Disorders of Immunoglobulins

The immunoglobulins are products of the complex and as yet not fully understood lympho-

cytic-plasmacytic series of cells. Consequently, disorders of the immunoglobulins are reflections of more basic abnormalities in their cellular system of origin. The immunoglobulin derangements can be divided into two broad categories: deficiency disorders and disorders associated with neoplasia.

In the light of clinical observations and recent experimental work on the thymus, a degree of order has been introduced into our concepts of the pathogenesis of the immunologic deficiency states. The specific immunoglobulin defects in these various disease states are shown in Table 3. Space does not permit further discussion of this involved and interesting subject which has been covered in a recent excellent review.¹⁷

Neoplastic proliferation of immunoglobulin-synthesizing cells usually results in the elaboration of paraproteins which appear in the serum or urine or both. The term "paraprotein" indicates that these proteins are structurally very similar to normal immunoglobulins; however, they are produced in excess and are usually restricted to a single molecular form. In addition, specific antibody function so far has not been demonstrated for any of the paraproteins. The paraproteinemias include plasmacytic myeloma, "monoclonal gammopathy" of unknown cause, Waldenström's macroglobulinemia, and heavy-chain disease.¹⁸

The protein abnormalities of plasmacytic myeloma are manifestations of alterations in protein synthesis in which a single type of globulin molecule or fraction thereof is formed by a clone of abnormal plasma cells. If the heavy chains and light chains are formed synchronously, an excess of whole molecules will appear in the serum as a myeloma peak. If there is asynchronism in chain production and light chains are produced in excess of heavy chains, there will be a myeloma peak concomitant with Bence Jones protein in the urine. If, in malignant dedifferentiation, the abnormal clone has lost the capacity to elaborate heavy chains, the only paraprotein to appear will be Bence Jones protein in the urine. Rarely (1% of cases), plasmacytic myeloma occurs without any detectable paraproteins. The frequencies with which the various paraproteins are observed are: IgG myeloma protein, 54%; IgA myeloma protein, 22%; Bence Jones protein

only, 23%. Bence Jones protein occurs in about 30% of cases with IgG or IgA myeloma protein.

Monoclonal gammopathy is an ill-defined group of paraproteinemias of unknown cause. It is sometimes associated with lymphomas or various carcinomas (rectum or prostate); occasionally it occurs without demonstrable underlying malignancy. This latter group may represent a latent phase of plasmacytic myeloma with the paraproteinemia preceding demonstrable plasma cell tumor by months or years.¹⁹

In Waldenström's macroglobulinemia, a more benign disorder than plasmacytic myeloma, excess protein, produced by abnormal "plasmacytoid lymphocytes," is associated with the IgM subclass. The increase in these macromolecules in the serum accounts for the hyperviscosity syndrome which is often seen in this disease.

Franklin's disease, or H-chain disease,²⁰ is a recently described paraprotein abnormality that presents clinically as a malignant lymphoma without evidence of bone involvement. The paraprotein, which has a molecular weight of approximately 55,000, occurs in the serum and in the urine. The urinary protein does not give the Bence Jones thermolabile reaction. Originally it was thought to be an excess of heavy chains, but it now appears that the paraprotein is more closely related, if not identical, to the Fc fragment of the papain digest.²¹

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Summary

The basic principles of electrophoresis, ultracentrifugation, immunodiffusion, and immunoelectrophoresis are described as a necessary introduction to the subject of the immunoglobulins. Antibody activity is confined to this group of serum proteins, which presently includes five subclasses: IgG (γ G); IgA (γ A); IgM (γ M); IgD (γ D); and IgE (γ E). Specific antibody activities have been identified within each of the subclasses except IgD. There is strong experimental evidence that the basic immunoglobulin molecule consists of four polypeptide chains (two light chains and two heavy chains) held together principally by interchain disulfide bonds. The light chains are of two types, K and L, and are indistinguishable from the Bence Jones protein that may occur in plasmacytic myeloma. The heavy chains are specific for each immunoglobulin subclass. Light chains and heavy chains must be combined for expression of full antibody activity. The immunoglobulin deficiency states and the paraproteinemias (for example, myeloma, monoclonal gammopathy, Waldenström's macroglobulinemia, and heavy chain disease) are briefly discussed in the light of this recent knowledge.

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References

1. Committee on Nomenclature of Human Immunoglobulins; Nomenclature of Human Immunoglobulins. Bull WHO 30:447, 1964.
2. Tiselius, A., and Kabat, E. A.: An Electrophoretic Study of Immune Sera and Purified Antibody Preparations. J Exper Med 69:119, 1939.
3. Deutsch, H. F., Alberty, R. A., and Costing, L. J.: Biophysical Studies on Blood Plasma Proteins. IV. Separation and Purification of a New Globulin From Normal Human Plasma. J Biol Chem 165:21, 1946.
4. Oudin, J.: L'analyse immunochimique du sérum de cheval par précipitation spécifique en milieu gélifié: Premiers résultats. Bull Soc Chim Biol 29:140, 1947.
5. Ouchterlony, Ö.: Antigen-Antibody Reactions in Gels. IV. Types of Reactions in Coordinated Systems of Diffusion. Acta Path Microbiol Scand 32:231, 1953.
6. Crabar, P., and Williams, C. A.: Méthode permettant l'étude conjuguée des propriétés électrophorétiques et immunochimiques d'un mélange de protéines: Application au sérum sanguin. Biochim Biophys Acta 10:193, 1953.
7. Fahey, J. L.: Antibodies and Immunoglobulins. I. Structure and Function. JAMA 194:71, 1965.
- 8-21. May be secured from the Grand Rounds Editor.

Most people would die sooner than think; in fact, they do so. — Bertrand Russell



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Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should be closely supervised and should be warned to report immediately fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage. Make regular blood counts. Discontinue the drug and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The most common are nausea, edema and drug rash. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. Infrequently, agranulocytosis, or a generalized allergic reaction may occur and require withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported but cannot definitely be attributed to the drug. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

Dosage in Osteoarthritis: The initial daily dosage in adults is 300-600 mg. in divided daily doses. When improvement occurs, dosage should be decreased to the minimum effective level; this should not exceed 400 mg. daily, and is often achieved with only 100-200 mg. daily.

For complete details, please refer to full prescribing information. 6562-VI(B)R

Availability: Tablets of 100 mg.



Geigy Pharmaceuticals
 Division of Geigy Chemical Corporation
 Ardsley, New York

Neurological Conference

Hemiparesis and Seizures in a Teenager

History

T HIS 17-YEAR-OLD boy was first referred to the University of Minnesota Hospitals in May 1965, for the treatment of a convulsive disorder. He had first experienced a grand-mal convulsion during a febrile episode at the age of 18 months. A left hemiparesis was present after this seizure and has persisted to the present time. Prior to this referral, the patient has been followed at the Sister Kenney Institute primarily for physical therapy of his left hemiparesis.

At age 13 the patient began experiencing grand-mal seizures. During the next two years he had between 10 and 20 grand-mal convulsions. An adjustment of his anticonvulsant medications from dilantin 100 mg. t.i.d. and phenobarbital 60 mg. b.i.d. to dilantin 100 mg. t. i. d. and mebaral 100 mg. q.i.d. resulted in complete control of his seizures. He has remained seizure-free to the present time.

Physically the patient still presents a problem in that his left hemiparesis has produced mild but significant contractures in his left upper and lower extremities. In addition, the question also arises about his future education, his occupation, and what recommendations and encouragement should be given him.

Neurological Evaluation

Dr. Robert Soll*:

Neurologically this patient presents with a mild left hemiparesis accompanied by hyperreflexia of both the left arm and the left leg and a Babinski sign in the left foot. The fact that there is no significant alteration of his sensation on the left side indicates that the neurological deficit is confined almost completely to the motor pathways. X-rays of the skull reveal no evidence of asymmetry which might have been expected if significant atrophy of the right hemisphere had been present since an early age. A recent electroencephalogram was interpreted as being moderately abnormal with multifocal slow spikes and waves in the frontal, temporal and mid-temporal regions on the right; however, there was

Sponsored by the U. S. Public Health Service Grant N2502A63. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals. The pediatric conferences are held every Wednesday from 1:00 to 3:00 p.m. The adult conferences are held every Thursday at 4 p.m. Co-ordinators for the project are Dr. Charles Branthaver and Dr. Edward Defoe in Pediatrics, and Dr. Robert Soll, in Adult Neurology. Held on January 19, 1967.

*Department of Neurology, University of Minnesota Hospitals.

Continued

diffuse slowing bilaterally. This record showed no significant change from a previous record taken in May 1965. It is anticipated that the patient will have to continue on anticonvulsant medication indefinitely. It would also be wise to discuss the general nature of seizures and their causes with the patient in order that he have a thorough understanding of his own condition. There are several excellent pamphlets that are available for patients to read that could be used to supplement this discussion.¹

Etiologically no cause was ever found to account for this patient's convulsive disorder and left hemiparesis. He apparently had had a perfectly normal birth without any complications and there has been no history of any serious injuries prior to the onset of his first seizure at age 18 months. In view of the rather abrupt appearance of a convulsion during a febrile episode, leaving as a sequela a left hemiparesis, one might speculate that the patient probably had an acute cerebritis which produced its most severe damage in his right cerebral hemisphere.

Physical Medicine Evaluation

Dr. Frank Meelhuysen*:

As the patient walks, he is unable to place his left heel down on the floor. This is the result of shortening of the triceps surae muscle on the left. If he attempts to stand with his left heel on the floor he has to lean forward with the upper half of his body to keep his balance. Passive dorsiflexion of the left foot with the knee extended is limited to 110°, representing a 20° loss of mobility. Attempting a similar maneuver with the knee flexed is limited to approximately 100°. Thus a contracture is present in both the gastrocnemius and the soleus, although most of the spasticity is in the latter.

Passive prolonged stretching of the calf musculature in time may accomplish adequate lengthening of the muscle; however, a more practical approach would be a tenotomy of the left Achilles tendon. This can be done quickly and would permit almost immediate ambulation of the patient. This procedure should be supplemented by fitting the patient with a short leg brace having an ankle stop at 90° which can serve as a "built-in" gastrocnemius muscle at the push-off phase of the gait cycle. It could also be used as a night splint in order to maintain the foot in a dorsiflexed position, thus maintaining the increased range of motions of the ankle. I would recommend an orthopedic consultation concerning the suggested tenotomy.

A further suggestion would be a reduction of the spasticity in the gastrocnemius and the soleus muscles of the left leg by means of motor point blocks using phenol solution. As you know this does not permanently reduce the spasticity but will relax the muscles for three to six months and permit passive stretching of those muscles more readily and effectively.

Moderate spasticity is also present in the left forearm flexors, both in the wrist and finger flexors. Very likely, continued passive stretching of these muscles should be sufficient to maintain their functional length. This can be accomplished by having the patient place his left hand with fingers and palm flat on a table, and keeping his elbow extended. He then leans forward causing the wrist to be forced into dorsiflexion. If passive stretching by this means proves to be insufficient, motor point blocks in some of the above mentioned flexors may also be helpful in facilitating the stretching.

*Assistant Professor, Physical Medicine and Rehabilitation, University of Minnesota Hospitals.

Psychological Evaluation**Dr. John Brantner^{*}:**

The patient has an average intelligence as indicated by a full scale WAIS intelligence quotient of 94. Since this is actually at the bottom of the average range, one would anticipate that he would do roughly C work in high school. On the other hand, he would have an extremely difficult time in most college courses. His level of abstract verbal ability is low. The Porteus Maze placed him at 100.

In regard to his personality, he is well controlled with no tendency toward impulsiveness or carelessness. Indications for brain damage are at best borderline and probably not significant. We have obtained two multiphasics on him within four days, which were almost identical except for a rather marked change in the level of psychic energy. This might indicate that he is sensitive to fatigue or possibly to his drugs. Otherwise the Minnesota Multiphasic Inventory showed him to be cheerful, optimistic, and reasonably socially oriented with no evidence of depression, anxiety, or concern over his physical condition. On the other hand, his level of social maturity is somewhat low. Interestingly, he was given the high school form of sentence completion test which has forty items in it. His answers included the word "girl" in 25 instances. This suggests that he is very concerned at the present time with his image of himself as a successful heterosexual, masculine kind of person.

Vocational plans are not going to be easy with this boy. His physical handicap probably will not be too difficult for him as far as his being a printer is concerned, since he is intellectually capable of doing this kind of work. Also according to his interest pattern, this is the type of work he should be directed into. In the interest test he clearly rejects the scientific area and is not greatly interested in developing verbal skills. Outdoor activities or active vocations such as printing would be good for him because his interest pattern definitely is that of a worker rather than an executive. It would be unfortunate for this patient to be encouraged to go to college, since his intelligence level is in the low average and his interest pattern does not fit well with college level work.

Social Service Evaluation**Miss Helen Kretchmer^{**}:**

The patient's counselor said the patient was a "Huckleberry-Finn" type of person at an earlier age but that he has changed recently. The patient had a summer job in a YMCA work training project before he entered senior high school. He apparently worked harder than the 14 other boys in this project which was provided for boys who had an inadequate home situation. His counselor was not certain why the patient had been chosen, although it may have been because he did not have a father at home. Tests at the YMCA revealed that the patient was limited in his reading skills but very capable when doing active work. In school his grades have been acceptable during this past year and he has been active in sports and Junior Achievement. His home-room teacher stated that he is a striver and that he tries to do the best he can despite his handicap. Although his pace is rather slow, he is dependable, quiet, and gets along well with others. According to his teacher, he apparently makes occasional gross mistakes, and his counselor noted that he is extremely poor in reading skills.

^{*}Associate Professor, Clinical Psychology, University of Minnesota Hospitals.

^{**}Supervisor, Social Service Department, University of Minnesota Hospitals.

Continued

The patient is an only child whose father has been out of the home for a long time. His stepfather has been gone since the patient was 12 years old. The grandparents are young, ages 62 and 61 years of age, and the patient has an uncle, age 22, who was reared as his brother. They all live together in an apartment building. The mother feels that the patient does very well in school and does not expect more of him than he is capable of doing. She works from 10:30 in the morning until 7:00 at night. The only problem with which the mother is concerned is her feeling that her son is "high strung." He gets very angry and upset on occasion when she tries to talk to him. Apparently he acts as though she knows nothing. This is beyond what she would ordinarily expect of a boy his age and she worries that it may lead to a more serious problem later. She would like some counselling in this regard.

Recommendations of the Community Service Conference

1. Avoid encouragement into advanced education or advanced training and rather promote the patient's interest in a vocational training area.
2. Continue seizure medications indefinitely and discuss the general nature of convulsive disorders with him in order to increase his understanding of his condition.
3. Consult orthopedics concerning a left Achilles tenotomy in order to lengthen his contractures; subsequently fit the patient with a short leg brace if a tenotomy is done.
4. Reduce the spasticity in the left gastrocnemius by motor point blocks.
5. Consider motor point blocks in the left forearm flexors if passive stretching proves to be insufficient in the upper extremity.
6. Send a summary to the patient's eleventh grade counselor.

Robert W. Soll, M.D.
University of Minnesota Hospitals

Participating in the conference were: Miss Helen Kretchmer, Supervisor, Social Service Department; Dr. John Brantner, Associate Professor, Clinical Psychology; Mr. David Osborn, Clinical Psychology Trainee; Dr. Frank Meelhuysen, Assistant Professor, Physical Medicine and Rehabilitation, and Dr. Robert Soll, Department of Neurology.

References

1. For example — Handbook for Patients and Handbook for Parents available from Ayerst Laboratories, 685 Third Ave., New York, New York 10017.

Mr. Barzun Comments

Catastrophic Remodeling

"With the first successful appendectomy in 1890, the abdominal cavity became the playground of the surgeon." A surgeon wrote this in all seriousness and self-satisfaction and his spirit lives on. Every convention discloses a busy group of specialists who discuss new and better ways of removing your liver without injuring your lights, and who deplore at the same time that half their cases are either inoperable or too far gone to yield anything but a technical victory to the operator. Lately one elderly man was completely remodeled inside at a cost of eight anesthetics, twenty-two hours total operating time, and a fee of \$20,450.

Is it possible—and I ask out of complete ignorance and humility—is it possible that if the patient had been under the lifelong care of one physician who knew his history, occupation, and mode of life, who stood in some permanent relation to him and was interested in his well-being, is it possible that this marathon with the scalpel could have been forestalled?

Jacques Barzun: *When the Doctor Is a Pill (In God's Country and Mine)* 1954



Grand Rounds

Electrical Conversion of Cardiac Arrhythmias *

NEIL HOFFMAN, M.D.
Medical Resident

THE USE OF electric current for terminating cardiac arrhythmias was first credited to Prevost and Battelli in 1899.¹ They applied strong electric currents to the exposed hearts of dogs to stop ventricular fibrillation. Little attention was given the procedure, however, until 1933 when Kouwenhoven reported that AC current applied directly to the exposed heart could terminate ventricular fibrillation.² This had limited clinical usefulness, however, until 1960 when Kouwenhoven demonstrated that, in the arrested heart, pressure over the lower sternum would maintain adequate blood flow to vital organs.³ This concept extended the time available for the effective use of countershock in ventricular fibrillation. In 1962, Zoll demonstrated that electric current applied to the intact chest wall was effective in abolishing certain arrhythmias, particularly in terminating ventricular fibrillation.⁴ Actually Zoll first used electric countershock in 1956 when he applied the current transthoracically in four patients with various arrhythmias, reporting one survivor.^{5,35} Beck,³⁴ in 1947, reported the first successful use of countershock with open-heart massage, a case in which the patient made a complete recovery.

Vulnerable Period

In 1940, Wiggers showed that an electrical shock, when applied to the intact heart, could cause the heart to go into ventricular fibrillation.⁶ He demonstrated that even a very small shock to a localized area of myocardium, when timed to the ascending limb of the EKG T wave, would cause most dogs' hearts to go into ventricular fibrillation. This time sequence in the cardiac cycle has been called the vulnerable period.

The vulnerable period for ventricular arrhythmias in man measures 30 milliseconds and just precedes the apex of the T wave. A similar vulnerable period has been noted for atrial arrhythmias and has been shown to occur during the down slope of the R wave. Vulnerable periods have been identified in other

Continued

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, Minneapolis, January 3, 1967.

mammalian hearts; all have the same duration and location.¹

In 1940, Wiggers also postulated that direct current would be better than alternating current because one could time a single shock to occur at the beginning of the cardiac cycle, and since the current would be stored in a capacitor, the variations in current strength available in the AC input line would be avoided.⁶

To compare the effectiveness of AC versus DC current, Lown in 1962 studied 55 dogs in sinus rhythm. He then applied equal voltage across an intact chest to these dogs and did not time the discharge to fall within any portion of the cardiac cycle. He showed that random shock would produce ventricular fibrillation in two percent of normal dogs. Of 20 dogs that received AC shocks seven died, while in 35 dogs with similar DC voltage there were no deaths.⁷ The fact that ventricular fibrillation occurred in two percent of normal dogs limited the clinical usefulness of this tool to humans. Lown then showed that by synchronizing the release of the discharge to fall during a safe part of the cardiac cycle, ventricular fibrillation could be avoided.^{8,9}

Prior to "cardioversion", drugs were the mainstay in the treatment of cardiac arrhythmias. The use of drugs presented many problems. The effective or toxic dose in an individual patient could not be predicted. Since the dosage varies, it is necessary to titrate safe increments of the drug at frequent intervals. This may be tedious and time-consuming to the physician, requiring constant monitoring.^{1,9,10,11,12,13,14} Because these drugs are time-consuming and carry a two-percent mortality rate, the simpler method of cardioversion, as popularized by Lown, became the accepted one.

Theoretical Basis for Cardioversion

Cardioversion for electrical arrhythmias is based on the following propositions:

The forces that initiate ventricular fibrillation are generally transient, but once started seem to be self-sustaining.

The sino-atrial node has the highest rhythmicity, and when an abnormal rhythm is momentarily stopped, the S-A node will assume its normal rate as a pacemaker.

Depolarization of the entire heart can be done across an intact chest.

Cardioverter^{1,7,9}

The cardioverter as popularized by Lown is composed of four separate parts:

D. C. Defibrillator

This has a specific wave form, calibrated in watt seconds, with enough energy to depolarize the heart across an intact chest. This delivers a monophasic pulse of 2.5 millisecond. The machine is calibrated from 0-400 watt seconds.

Synchronizer

This permits the discharge at a preselected phase in the cardiac cycle, using the R wave as a trigger point to discharge the electric shock, thus avoiding the vulnerable period.

Cardiometer

This allows a permanent ECG to be taken and provides an R wave as refer-

ence for the synchronizer. There is also an ECG reversal switch to artificially make an S wave appear as an R wave.

Cardioscope

This provides an oscilloscope for monitoring purposes.

Beneficial Effects of Normal Sinus Rhythm

Most studies in comparing atrial fibrillation to sinus rhythm show definite improvement in cardiac performance when sinus rhythm is restored. *Cardiac output increases, ventricular rate with exercise decreases, and stroke volume increases.*^{15,16,17,36} Rodman¹⁸ studied 36 patients with cardiac catheterization before and five to seven days after restoration of sinus rhythm. He showed that stroke volume was increased from 35 millimeters to 77 millimeters (45%) with no essential change in heart rate. This emphasizes that the hemodynamic benefits attained with restoration of sinus rhythm cannot be attributed entirely to reduction of heart rate. Knox showed that even in well controlled atrial fibrillation the rise in left ventricular pressure is significantly higher in patients with atrial fibrillation than in those with sinus rhythm. It has also been established that patients with atrial fibrillation with no other evidence of heart disease may develop cardiac dilatation and failure.¹⁹

Indications for Cardioversion

Patients Who Should Undergo Cardioversion^{11,18,20,21}

1. Patients who are fibrillating and have a history of systemic emboli. As this is a prime indication, every effort should be done to maintain sinus rhythm.
2. Patients in congestive heart failure who are in atrial fibrillation and still have significant cardiac decompensation. Here, repeated reversions over the course of years may be helpful.
3. Patients with cardiac decompensation after an acute episode, e.g., acute myocardial infarction, where a supraventricular arrhythmia may be life threatening. Many investigators feel that cardioversion in these poor-risk patients without anesthesia is better than prolonged ineffective medical management.
4. Patients with ventricular tachycardia.
5. Patients with ventricular fibrillation.

Relative Contraindications because of Questionable Value^{10,20}

1. Slow atrial fibrillation without digitalis. This type of atrial fibrillation is generally associated with ischemic heart disease.
2. Intolerance to anti-arrhythmic drugs. Even though electrical conversion will restore sinus rhythm an anti-arrhythmic drug is generally necessary for maintaining this rhythm. One of our patients (#6) was found to be intolerant to Pronestyl and quinidine; after her second cardioversion she is being maintained on dilantin.
3. Previous cardioversion without improvement and early recurrence.
4. Benign atrial fibrillation of long duration. Data in this group fail to show any hemodynamic benefit in restoration of sinus rhythm.²² Oram reported some

Continued

benefit²³; but since the morbidity is low and these patients are generally asymptomatic the indications for cardioversion are equivocal.

Relative Contraindications—Defer to Later Date^{8,20,25}

1. Recent onset of supraventricular tachycardia. Most paroxysmal arrhythmias will revert within one week; therefore Morris²⁰ suggests drug therapy for one week.
2. Candidates for cardiac surgery who are stable.
3. Postoperative cardiac patients. Experience here has shown that the recurrence rate is less if one waits until the postoperative convalescence is nearly complete before attempting to restore sinus rhythm.^{20,21,24}
4. Patients with atrial fibrillation, secondary to hyperthyroidism (over 50 percent) will revert to sinus rhythm with the return of a euthyroid state.
5. Patients with recent systemic emboli. Here an eight-week period of anticoagulation is advised to give the mural thrombosis time to adhere and prevent dislodgment at the time of cardioversion.

Absolute Contraindications to Cardioversion^{17,20}

1. Digitalis intoxication. Electrical reversion of these arrhythmias results in a higher mortality rate because of an irritable myocardium that may produce multifocal PVC's or Stokes-Adams attacks.
2. Complete heart block. Here restoration of sinus rhythm will not alter the hemodynamic effects. Also this type of individual tolerates anesthesia poorly, and the risk from embolization is low.
3. Angina, relieved by the onset of atrial fibrillation.
4. Recurrent episodes of supraventricular tachycardia. This may be so uncomfortable that it seems best to leave these patients in atrial fibrillation.
5. Sinus tachycardia.

Technique of Cardioversion (Table 1)

Cardioversion is generally done using the Lown cardioverter in the following manner. Digitalis should be discontinued for 48 to 72 hours and an attempt made to control congestive heart failure with bedrest, diuretics, and a low salt diet. Quinidine therapy in doses of 1.2 grams to 1.6 grams should be given in individual doses 24 hours prior to cardioversion. The patient is not allowed food or fluids orally the day of cardioversion, except for the anti-arrhythmic agent. If general anesthesia is to be used, atropine just prior to induction helps control secretions.

The patient is then connected to the cardioverter with the operations switch turned to the monitor position. An appropriate ECG lead is decided upon so that a suitable R wave can be used as a trigger. The height of this wave can be artificially increased by using the gain control. If an S wave is to be used, the ECG reversal switch must be used, so that this negative S wave will appear on the screen as a positive deflection. The operations switch is then turned to the cardioverter position. At this time the signal light will blink each time the R wave has enough magnitude to fire the machine. This is an automatic synchronizer built into the machine. The synchronizer will trigger the machine so that the shock will fall 0.07 seconds after the R wave. Thus the entire shock

is delivered away from the vulnerable period, which for ventricular arrhythmias is at the apex of the T wave. There is a small danger of precipitating atrial arrhythmias, but in Lown's large series only two episodes of atrial fibrillation occurred, both responding to reconversion.²⁶

The proper voltage is then selected. Generally 100 watt seconds is used as the initial voltage. The paddles are well lubricated and placed in the left infra-scapular position posteriorly, and in the fourth right interspace (V_1 pos.) anteriorly. The discharge button is then depressed and held until the shock is obtained. The voltage is then turned to zero reading and the reset button depressed. This will empty the capacitor of any remaining charge. If the patient remains in an undesired arrhythmia the energy level is increased by increments of 50 watt seconds until the maximum level of 400 watt seconds is reached. If the patient does not convert with a voltage of 400 watt seconds, it is suggested the procedure be terminated.

Use of Anesthesia

Recently the need for anesthesia has been questioned. Several investigators show series of repeated cardioversion without anesthesia.^{12,14,17,27,28} Lown suggests that voltages of 100 watt seconds or less are well tolerated by the patients; however, anesthesia does seem to be the procedure of choice. Anectine and other muscle relaxants seem to potentiate the action of quinidine and therefore should not be used.

Anticoagulants

The question of anticoagulants is not fully resolved. No series can show an

TABLE I
Summary of Technique of Cardioversion

SUMMARY OF TECHNIQUE OF CARDIOVERSION	
1.	Control of congestive heart failure.
2.	Stop digitalis therapy 48 to 72 hours prior to cardioversion.
3.	Anti-arrhythmic drug: usually quinidine 300 to 400 mg. q6h. p. o.
4.	Nothing per mouth for 12 hours prior to procedure except for oral anti-arrhythmic drug.
5.	No specific premedication necessary.
	a. Atropine, 0.6 mg., parenterally just before cardioversion if anesthesia is to be used.
6.	Anesthesia, optional; brevital, penethal.
7.	Paddle placement.
	a. Anterior fourth interspace just to the right of the sternum (V_1 position on ECG).
	b. Posterior at the left infrascapular area.
8.	Find representative ECG lead. Lown cardioverter has ECG reversal switch so that either R or S wave of ECG can trigger charge.
9.	Turn switch from monitor to cardioverter.
10.	Set desired voltage (usually start with 100 watt seconds).
11.	Press discharge button and keep depressed until shock is delivered.
12.	Turn intensity switch to zero and press reset button; now reading on voltage scale should read zero.
13.	Resume anti-arrhythmic agent.
14.	Resume digitalis in 24 hours if necessary.

Continued

GRAND ROUNDS

advantage for using them.^{1,10,14,17,26,27,28} Morris reviewed 784 cases of cardioversion and found systemic emboli in 1.1 percent. It is significant that only one appeared immediately after cardioversion. Generally they occur two to 10 days after the procedure. He advises anticoagulation only if there is a history of previous embolism and suggests their continuance for two to three weeks following cardioversion.²⁰

Complications

The most common complications following cardioversion are transient arrhythmias. These are enhanced by digitalis toxicity. Killip¹⁰ reports one case of ventricular fibrillation produced when an artifact triggered the shock.

Cardioversion is considered safe. Kong²⁹ reported one patient who underwent 140 D.C. shocks within a 69-hour period. This patient died but at autopsy there was no evidence of myocardial injury. In over 1,200 reported cases there was only one ECG compatible with injury, but in that case the serum enzymes were normal.³⁰ In the absence of digitalis toxicity Morris²⁰ reports in 784 episodes an incidence of ventricular arrhythmias of 0.5 percent, with no mortality.

Results

The reported results in conversion of atrial fibrillation to normal sinus rhythm run 91 to 95 percent, and for conversion of atrial flutter to sinus rhythm about 94 to 100 percent.^{8,12,20,26,31,32,33} Generally long-term follow-up of these patients has been disappointing. Only about 50 to 60 percent are still in sinus rhythm at the end of nine months.^{10,11,20,28} Factors that seem helpful in determining who will remain in sinus rhythm are: (1) The etiology of the arrhythmia. (2) The duration of the arrhythmia. (3) The functional classification of the patient at the time of cardioversion.

Patients with rheumatic heart disease, with lesions other than mitral stenosis, and those with ischemic heart disease and hypertensive heart disease frequently revert to atrial fibrillation. Patients with mitral stenosis seem to show a higher percentage of maintaining sinus rhythm. Also noted is the fact that if atrial fibrillation is present for less than one year, there is a greater chance for continuation of sinus rhythm. The presence of functional class III or IV in cardiac patients with fibrillation does not generally maintain sinus rhythm.^{1,9,20,27}

Hennepin County General Hospital Series (Table 2)

This series is not a complete review of our experience. From November, 1965, to December, 1966, our series includes nine patients, with one patient undergoing conversion on two separate occasions. Six of our nine patients were thought to have valvular disease, one with isolated aortic stenosis. One patient remained in sinus rhythm for only one month, stopped taking his medications, and was thought too unreliable for reconversion. Another patient (#7) had rheumatic heart disease and no detectable mitral lesion. He also reconverted to atrial fibrillation in six weeks. The other seven patients were followed from a period of one month to 13 months and have remained in sinus rhythm. The average time duration in our patients from onset of fibrillation to cardioversion was less than 12 months, but one patient was fibrillating for at least three years before conversion. He reverted to atrial fibrillation in one month. One patient had a mitral valve replacement and was converted two and one-half months after surgery. All our patients are on maintenance quinidine therapy averaging

ELECTRICAL CONVERSION OF CARDIAC ARRHYTHMIAS

1.2 grams per day except for patient #6, who was found to be intolerant to quinidine and pronestyl and is being satisfactorily maintained on dilantin.

TABLE 2
Experience at Hennepin County General Hospital

Patient	Age	Onset of Atrial Fibrillation	Date of Cardioversion	Follow-up	Anticoagulants Used	Sinus Rhythm
1. C. J.	76	11/62	4/65	1 mo.	No	No
2. H. M.	54	?	11/66	2 mo.	Yes	Yes
3. S. B.	62	7/65	1/66	12 mo.	No	Yes
4. J. S.	60	?	10/66	3 mo.	No	Yes
5. R. L.	60's	7/65	4/66	9 mo.	No	Yes
6. M. F.	60	?	11/65	9 mo.	Yes	No
			(2-1/2 mo. post mitral valve)			
		8/66	8/66	5 mo.	Yes	Yes
		(Now on dilantin)				
7. J. B.	61	?	11/65	1 mo.	Yes	No
8. W. M.	52	4/66	12/66	1 mo.	Yes	Yes
9. M. H.	54	?	12/66	2 wk.	No	No

Our success rate for immediate conversion was 100 percent. One patient required 250 watt seconds, the others converting generally after one shock at 100 watt seconds. Our follow-up period averages six and one-half months per patient and shows 66 percent of our patients to be in sinus rhythm. Three of our patients were anticoagulated by no specific criteria and no case of embolism was noted in our series. All of our patients had general anesthesia, and none reported undue chest discomfort or erythema following the procedure. When serum enzyme levels were obtained following cardioversion they were normal. Transient arrhythmias were noted, but no sign of myocardial damage was seen in follow-up ECG's.

Summary

Generally the initial conversion success rate is excellent with most series reporting 50 to 60 percent remaining in sinus rhythm for nine to 12 months. Anticoagulants were found not to alter morbidity or mortality. They are used generally for "high risk" patients, those with a previous history of embolic phenomena. Embolization has been reported at from 0.6 percent to two percent with no relationship to anticoagulants. Digitalis toxicity greatly enhances the morbidity of cardioversion. The most common complication is transient arrhythmias. Cardioversion seems to be the method of choice for conversion of atrial fibrillation and flutter.

References

1. Lown, B.: *Mod Conc Cardio Dis* 33:863, 1964.
2. Hooker, D., Kouwenhoven, W., and Langworthy, O.: *Amer J Physiol* 103:444, 1933.
3. Kouwenhoven, W., Jude, J., and Knickerbacker, G.: *JAMA* 173:1064, 1960.
4. Zoll, P., and Linenthal, A.: *Circulation* 25:596, 1962.
5. Zoll, P. M., et. al.: *New Engl J Med* 254:727, 1956.
6. Wiggers, C., and Wegrea, R.: *Amer J Physiol* 128:500, 1940.
7. Lown, B., Neuman, J., Amarasingham, R., and Berkoutz, B.: *Amer J Cardiol* 10:223, 1962.

8-36 May be secured from the Grand Rounds Editor.

I am suffering from my old complaint, the hay-fever. I melt away in nasal and lachrymal profluvia. My remedies are warm pediluvium, cathartics, topical application of a watery solution of opium to eyes, ears, and the interior of the nostrils.

—Sydney Smith

A large, dark, grainy microscopic image showing numerous spermatozoa with long, wavy tails. In the upper left corner, there is a smaller, rectangular inset showing a different microscopic view, possibly of cervical mucus or a different type of cell.

New view of an oral contraceptive at work

Although suppression of ovulation remains the primary mode of action of oral contraceptives, newer knowledge indicates that products like Norinyl-1 — a combination of both low-dosage progestogen and estrogen for the full treatment cycle — may provide multiple action that helps explain their unexcelled record of contraceptive effectiveness. This report explores the possible secondary protective mechanisms offered by combined hormonal administration.

Accumulating evidence has indicated that sparse, highly viscous cervical mucus has a possible adverse effect on the motility and survival of spermatozoa.

The estrogen-opposing progestational ingredient of Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.) changes the usual mid-cycle picture of a thin, watery cervical mucus. The result — a built-in barrier that appears to inhibit sperm from reaching the ovum should one be released. The inset in the adjoining photograph shows immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

How the estrogen-opposing action of Norinyl-1 creates cervical mucus that may be hostile to sperm penetration

Normally, estrogen activity during the fertile midcycle stimulates the production of a profuse and watery cervical mucus that permits maximum sperm motility and promotes penetration.

But what happens when Norinyl-1 is administered? Its potent progestogen, norethindrone, opposes estrogen stimulation of cervical mucus. Consequently, the amount of mucus decreases and its viscosity increases. This results in a sparse but thick mucus barrier that appears to diminish the vitality of the sperm and to impair its powers of penetration.

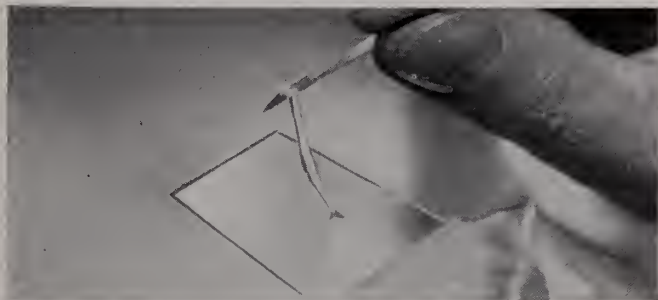
The role of viscous cervical mucus as a secondary action of Norinyl-1

In a report on 89 patients taking this medication,* cervical mucus obtained from cycle day 5 to cycle day 29 appeared scant and thick and exhibited little or no Spinnbarkeit.

In the opinion of this investigator, the effect on cervical mucus may be sufficient to prevent conception.

*Cohen, M. R.: Symposium: Mechanisms of Action of Low Dosage Oral Contraceptive, Yale University Medical Center, New Haven, Conn., April 6, 1967.

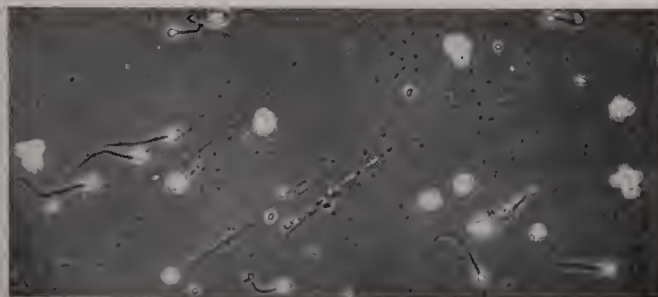
Normal cervical mucus at midcycle in untreated patient is known to permit sperm motility... promote sperm penetration.



Cervical mucus is thin and watery with a stretchability (Spinnbarkeit) of 15 to 20 cm.



Thin, watery mucus crystallizes into this well-defined, fernlike pattern within a minute.

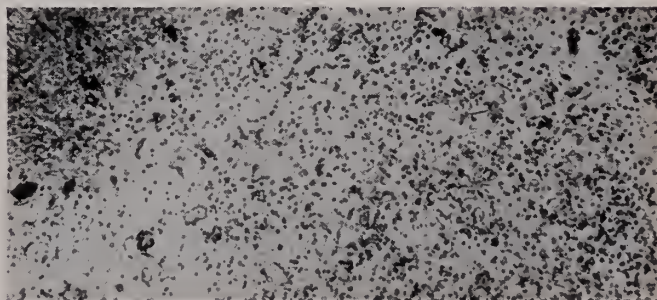


Spermatozoa appear healthy, are active and freemoving.

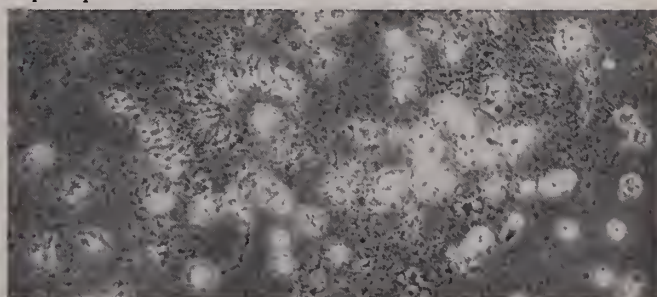
Viscous cervical mucus at midcycle produced by Norinyl-1 appears to impair sperm vitality... inhibit penetration.



Cervical mucus is scanty, thick and viscous. Spinnbarkeit is 1 cm. or less.



In thick, viscous cervical mucus the fern pattern is poorly defined or absent.

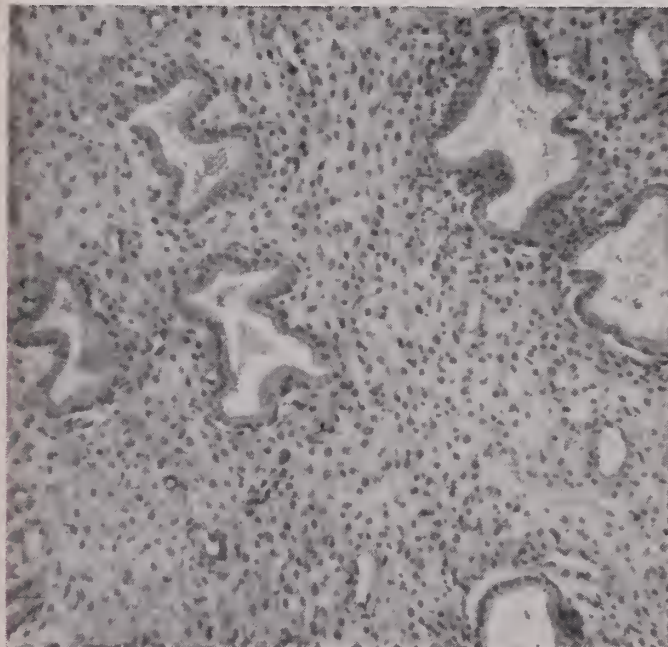


Immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

How Norinyl-1 alters normal endometrial responses— another possible protective mechanism

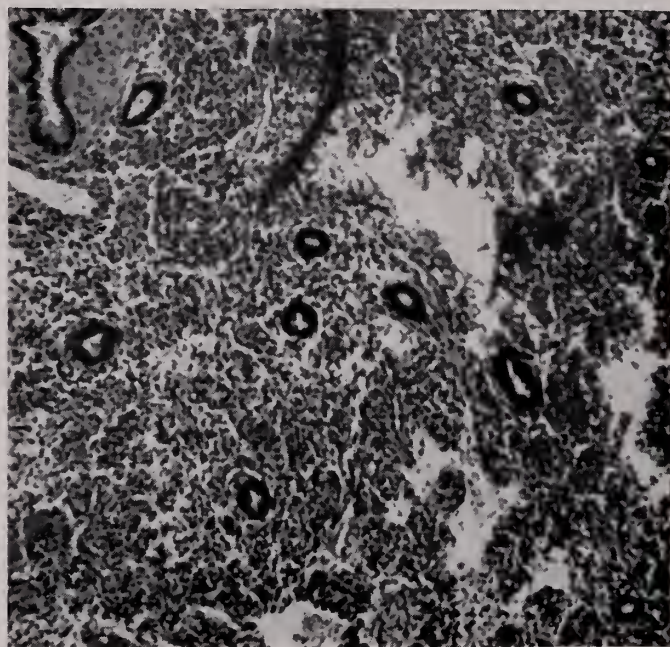
Let us suppose that an ovum is released—as occurs in an occasional, rare case—and somehow a sperm succeeds in penetrating the cervical mucus barrier. Should this come about, one additional action of Norinyl-1 may protect the patient from unwanted pregnancy. The theory is that progestogen intake makes endometrial tissue unreceptive to implantation.

Endometrium of
untreated patient



Normally, the endometrium progresses through a proliferative phase stimulated by estrogen and a secretory phase stimulated by progesterone. During the secretory phase the endometrium is receptive to the fertilized ovum.

Endometrium produced
by Norinyl-1



When Norinyl-1 is administered its progestogen component—norethindrone—accelerates the secretory phase and suppresses glandular and vascular development.

effective fertility control
on half the previous dosage
maintains ratio
of the established
norethindrone/mestranol
combination
lower cost

new Norinyl-1[®]

(norethindrone 1mg. $\bar{c}$ mestranol 0.05mg.) tablets

Reduction of oral contraceptive dosage to lowest effective levels has become a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now available in a new strength in which both norethindrone and mestranol are reduced 50 percent. Studies show that Norinyl-1 achieves fertility control with only 1.05 mg. of combined progestogen and estrogen per tablet.

Norethindrone was first reported for use as a progestational agent in human beings in 1955. Norethindrone 2 mg. with mestranol 0.1 mg., as an oral contraceptive, is currently in use by over 2,000,000 women. Clinical experience now establishes that Norinyl-1 also amply meets the criteria of reliability and safety.*

*Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965.

PRESCRIBING INFORMATION

Contraindications: 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

Warnings: 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of Norinyl-1 in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

Precautions: 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with Norinyl-1. Therefore, if such tests are abnormal in a patient taking Norinyl-1, it is recommended that they be repeated after the drug has been withdrawn for 2 months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibroids may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac, or renal dysfunction, require careful observation. 5. Although a cause and effect relationship has not been established, Norinyl-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, as in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are

indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged Norinyl-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Norinyl-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. A cause and effect relationship has not been demonstrated. 11. Because of the effects of estrogens on epiphyseal closure, Norinyl-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask the onset of the climacteric. 13. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

Side Effects: The following adverse reactions have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma, breast changes (tenderness, enlargement and secretion), loss of scalp hair, change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, erythema multiforme, erythema nodosum, hemorrhagic eruption, migraine, rash (allergic), itching, rise in blood pressure in susceptible individuals, mental depression.

The following occurrences have been observed in users of oral contraceptives. A cause and effect relationship has not been established: thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory results may be

altered by the use of oral contraceptives: increased bromsulphalein retention and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in T₃ values), metapyrone test, pregnane-diol determination.

Other side effects reported to have occurred in association with use of this drug are dizziness, hirsutism, pains in legs, back, chest and abdomen, dysuria, drowsiness, vaginal discharge, libido increased and decreased, eruptions, hypermenorrhea, hypomenorrhea, increased appetite, G.U. infections, varicose veins, abdominal fullness, acne, headache, nervousness, allergies, blurred vision, pain in eyes, and itching in eyes. For complete clinical data, see package insert.

Dosage and Administration: 1. One tablet of Norinyl-1 is administered orally for 20 days beginning on day 5 of the menstrual cycle. (Count day 1 of the cycle as the first day of menstrual bleeding.) Repeat this dosage schedule for each cycle. 2. If no menstrual period occurs after a cycle of treatment (20 tablets) in which patient adhered to the schedule, the patient must be instructed to resume taking the Norinyl-1 tablets 7 days after the previous 20-day course was completed. For example, if the last pill of a previous cycle had been taken on a Sunday, then a new cycle of treatment should begin on the following Sunday. 3. In the postpartum woman, it is recommended that the first cycle of treatment should begin on day 5 of the first menstrual cycle. However, Norinyl-1 should not be administered during lactation.

Availability: Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.)—Dispensers of 20 and 60 and bottles of 250 tablets.

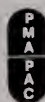
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facilities of medical schools and teaching hospitals. Such cooperation leads toward more effective care of more patients—the common goal of medical and pharmaceutical research—toward reduction in the cost of disease, toward increase in useful longevity.

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Abstracts, Briefs and Commentaries

ACUTE APPENDICITIS IN INFANTS THIRTY-SIX MONTHS OF AGE OR YOUNGER

Acute appendicitis in infants three years old and younger is quite uncommon; yet the mortality rate for this age group (6.7%) was nearly three times that for the entire 6,915 cases of the disease seen between 1953-1963 at the Los Angeles County Hospital.

Of the 30 cases reviewed 76.6% were ruptured at the time of surgery. There were two deaths. The authors stress a careful abdominal examination in a quiet child in order to detect objective evidence for appendicitis. This often requires medication. The hypohydrated, toxic infant must be carefully prepared prior to surgery.

Five factors contributing to a delay in diagnosis are: (1) failure to consider the possibility of appendicitis; (2) a poor history; (3) the frequency of vomiting in extra-abdominal conditions in infants; (4) antibiotics masking the disease; (5) more rapid progression of the disease in infants than in adults, resulting in earlier perforation.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

Fields, Irving A., and Cole, Norman M.: Acute Appendicitis in Infants Thirty-Six Months of Age or Younger. Ten-Year Survey at the Los Angeles County Hospital. *Amer J Surg* p. 269, February, 1967.

DEFINITIVE SURGICAL THERAPY FOR PERFORATED PEPTIC ULCER A REVIEW OF FIFTY-TWO CONSECUTIVE CASES

Definitive surgery to correct the ulcer diathesis may be performed in the presence of acute perforation with no increase in risk over simple closure or elective surgery and with equally satisfactory results. Fifty-two consecutively operated cases (minus 2) with a mortality of 1.9% are the basis for this report.

The author has followed all of his patients from fifteen months to six years with an average of three years. There was an incidence of dumping in 4%. Comparisons are drawn between this series and other published reports.

There is insufficient data in this report to warrant the author's conclusions. The time interval between perforation and surgery has not been studied. This would seem to be mandatory in a fair comparison of series. How can one judge the adequacy of an acid-ablative procedure with such a short followup?

Such a fine series of surgical cases so expertly handled deserves a more critical analysis. The author's conclusions may be right.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

Tolley, John A.: Definitive Surgical Therapy for Perforated Peptic Ulcer—A Review of Fifty-Two Consecutive Cases. *Amer J Surg* 113:3:327,

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IN BRIEF.

Contraindications: History of previous hypersensitivity to oxazepam. Oxazepam is not indicated in psychoses.

Precautions: Hypotensive reactions are rare, but use with caution where complications could ensue from a fall in blood pressure, especially in the elderly. Withdrawal symptoms upon discontinuation have been noted in some patients exhibiting drug dependence through chronic overdose. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose; excessive, prolonged use in susceptible patients (alcoholics, ex-addicts, etc.) may result in dependence or habituation. Reduce dosage gradually after prolonged excessive dosage to avoid possible epileptiform seizures. Withdrawal symptoms following abrupt discontinuance are similar to those seen with barbiturates. Caution patients against driving or operating machinery until absence of drowsiness or dizziness is ascertained. Warn patients of possible reduction in alcohol tolerance. Safety for use in pregnancy has not been established.

Not indicated in children under 6 years; absolute dosage for 6- to 12-year-olds, not established.

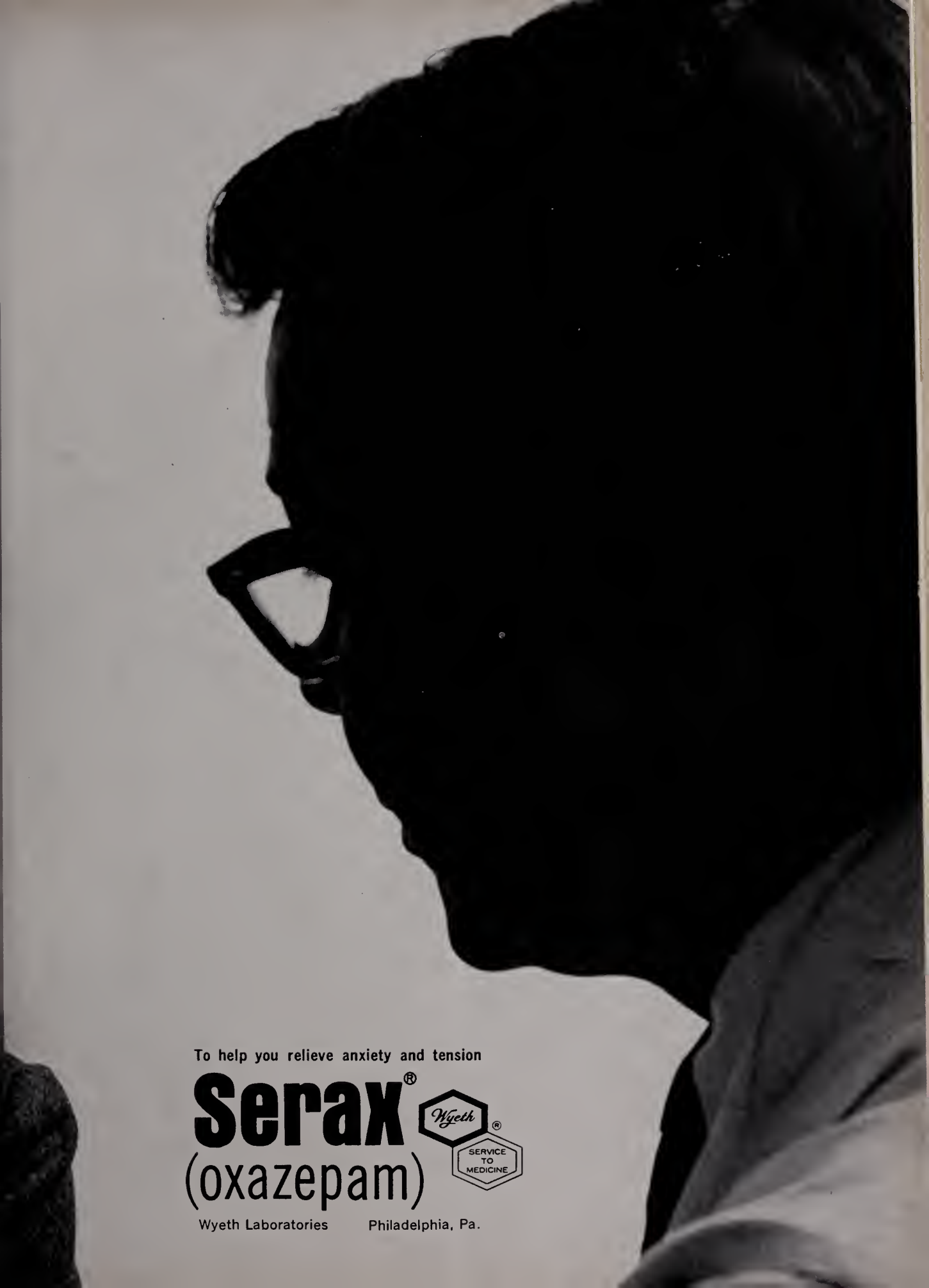
Side Effects: Therapy-interrupting side effects are rare. Transient mild drowsiness is common initially; if persistent, reduce dosage. Dizziness, vertigo and headache have also occurred infrequently; syncope, rarely. Mild paradoxical reactions (excitement, stimulation of affect) are reported in psychiatric patients. Minor diffuse rashes (morbilliform, urticarial and maculopapular) are rare. Nausea, lethargy, edema, slurred speech, tremor and altered libido are rare and generally controllable by dosage reduction. Although rare, leucopenia and hepatic dysfunction including jaundice have been reported during therapy. Periodic blood counts and liver function tests are advised. Ataxia, reported rarely, does not appear related to dose or age.

These side reactions, noted with related compounds, are not yet reported: paradoxical excitation with severe rage reactions, hallucinations, menstrual irregularities, change in EEG pattern, blood dyscrasias (including agranulocytosis), blurred vision, diplopia, incontinence, stupor, disorientation, fever and euphoria.

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Religion in American Life

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Annual Meeting

Presidential Address - 1967*

Mr. Speaker, members of the House of Delegates, and Guests: I come before you today with a plea for patience such as you have never had to demonstrate in times previous. This past year has seen a start of a system of medical practice which the world has never seen attempted. There are many countries who have tried the well known system of government taking over the control of medicine lock, stock and barrel. We know that these systems have not worked in the public or professional interest, that is, we know that medical care has deteriorated in many ways under such a system, certainly with great loss of freedom to practice, such as we know it to be in our own country.

Government Interest in Medicine

We are attempting a great experiment, wherein government is seeking to purchase medical care from the private sector of medicine through third party arrangements, which have turned out to be many and varied, each state having tried to work out arrangements of its own, which makes each state's plan almost unique unto itself. This part is good, because out of all the conflagration that is going on now in all our efforts throughout the country to make it work, we are running into a host of hitherto unforeseen problems. This is why I plead with you as physicians, and I could just as well address myself to the public and government as well, to have great patience while we continue to work on these problems until they are satisfactorily solved. So many situations are new and without precedent that it is no wonder we have run into snags.

Bureaucracies

Let me make this point extremely clear. It is up to us to make it work, because, if we

don't, you can be sure that the government will then take over as they have done in England, and many other places.

We should not reject these new regulations out of hand, but make a courteous effort to work out our problems with all parties involved, The Federal Bureau of Family Affairs, Social Security Administration, our Public Welfare Department and the carriers. The carrier is acting as a buffer between government and medicine, and those who regard them in the same light as government are wrong. They should be regarded as part of the private sector of medicine. If the government has to take this entire effort over, it will get rid of the carriers, you can be sure.

Let me discuss some of our own experiences here in Minnesota during this past year. What have been our own unique problems?

Assignments

First of all, we were all asked to take assignments when it came to dealing with our welfare patients. This is the prime method, and really the only one, which is being used throughout the country as a method for collection from this particular group of patients. We were allowed to bill all other patients over 65 who had Medicare directly, collect from them, and they in turn could recover from the government that portion to which they were entitled by law, through the carrier arrangement. A high percentage of physicians throughout the country accepted this assignment method for Welfare Patients and apparently have found it to be satisfactory thus far.

Direct Billing

However, there is a sizable number of physicians here in Minnesota and in many other states who have refused to go along with this idea, and would not accept assignment. Through our own Task Force on Medicare, chaired so

*Given before the House of Delegates, May 14, 1967, Duluth, Minnesota.

Continued

ably by Dr. John Falls of Red Wing, we were able to obtain arrangements through the Department of Public Welfare to have the same direct billing method used for welfare patients. This meant that the welfare recipient had to either scrape the money together, pay the doctor, get a receipted bill and present this to his welfare board, so that they could pay their share, and also collect from the carrier the share to be paid by the Federal Government, or accept a promissory note so that a receipted bill could be given to the welfare patient. This proved to be a very awkward arrangement, but at least it was made possible by the efforts of Dr. Falls' Task Force.

This was not sufficient, however. Many physicians wished to continue to deal with their county welfare boards just as they had done for many years, and had developed reasonably satisfactory arrangements for the most part. This meant that they wanted to continue to bill their welfare departments directly, let the welfare people work out their own arrangements with the carriers for getting the Federal Governments share for them to utilize, and so simplify their own bookkeeping, feeling that the bookkeeping chore should properly be done by the welfare department, leaving them as free as possible to use their own time to the best advantage practicing medicine.

Changing Medical Economics

A striking change has occurred in medical economics in the past 20 years.

Paramedical Personnel

Most physicians are being called upon to see many more patients than they did years ago, and can't push themselves any harder. They have been able to do this by employing more so-called paramedical personnel, which has driven overhead up. Paper work has increased tremendously, but most physicians prefer to deal with their local people, and it is our obligation to assist them in doing this.

Legal Obstructions

It is at this point that we are now hung up. In order to do this, there must be amendments to our Title 18 and 19 laws. It could also be corrected by a rather simple change in the Fed-

eral law, and this is being worked on in Washington. That change in the Federal law would be to strike out the requirement for a receipted bill, and allow the physician to send his bill to both the county welfare department as well as the carrier. These two could then work out their own arrangements so that each could pay his share of the bill, and it could all be done without any use of assignment whatsoever.

Now there are many physicians in this state who do not agree that this assignment business holds the dangers or potential dangers that some seem to think, and would just as soon accept the assignment and go along with the prescribed method which the government is asking throughout the country. We have been asked by our own welfare people, why are the Minnesota physicians so different than any others in the country that they would refuse to accept assignment?

Private Practice vs. Government Employee

Let me give you some examples. For the greater part of my professional life I have been in the private practice of medicine, but now am an employee of the state government, yet you have honored me by electing me as your president without fear, I hope, that I would suddenly transfer my allegiance toward government medicine. It is obvious to me that service can be rendered from both positions, each respecting the other. You have given our Distinguished Service Medal to a long time state government employee, Dr. Robert N. Barr, Executive Secretary of our State Board of Health, who has steadfastly upheld the private sector of medicine. Dr. Valentine O'Malley has worked in the disability section of the Social Security Administration and has up-graded that governmental department, yet has maintained the closest relationship with private practitioners. One of our excellent recent presidents, Dr. Donald McCarthy came from a long full time post with the Veterans Administration to take that office. To me this indicates a trust in many physicians in government service at this level. We prefer to deal with physicians and non-physicians at these more local and state levels where we can know them, rather than with unknowns in Washington.

There is such marked disagreement over this taking of assignment, not only in Minnesota,

but elsewhere, that I think it is absolutely necessary for those of us in positions of medical leadership to try our best to uphold the rights of individual practicing physicians, and try to achieve that which they desire, if at all possible. This is exactly what we have been trying to do, and have gotten ourselves in many difficulties as a result.

The Right to Refuse

These physicians have billed their welfare boards, knowing that they could not be paid, and will not be paid until this matter can be settled legislatively, either by our own state legislature, or by Congress, as I have indicated. I also know that certain welfare boards have urged their physicians to change their minds and accept assignments, telling them that they could not be paid for any bill that is more than one year old, which may be true. The physicians are adamant, however, and there have been some rumors, and I would pray that they are no more than rumors, that these men would eventually refuse to render medical care to their welfare patients except for emergency care, because they were not getting paid. This would be utterly unthinkable, in my opinion, and would badly tarnish the image of the medical profession. It would not, in my opinion, solve the problem, but would, in fact, compound it, by placing us right in the same category as tradesmen, and take us out of the professional status entirely. Lest I be misinterpreted in making this statement about "tradesmen", let me say that these good people in our society have every right to do as they have done many times in improving their own lot by striking, but their work does not involve human life as directly as ours does, and therefore we are in a totally different situation. No matter what might happen in the economic affairs of any physician, I cannot believe that he should ever refuse to take care of a certain group of his patients purely on an economic basis. I hasten to add, however, that any physician in private practice may say "no" to the request for medical care from a single patient or his family for purely personal reasons. This has always been true. But to turn down the care of an entire group of his patients, such as those who have the misfortune to be on welfare would be utterly unprofessional, in my opinion, and would

be absolutely unethical. It would be labeled a STRIKE.

The Family Physician

I have spent a considerable amount of time in talking about this dilemma in which we find ourselves, because I think it deserved it. There are other matters which should be talked about too. One of the most urgent is the matter of Medical Manpower. As time has gone on, we all know that the Family Physician has become an increasingly scarcer entity. We must make the best use of the doctors in all fields, and this means that governmental agencies, in working with all of us on these new Medicare problems, *must free us from as much paper work as possible*, and allow us to spend as much of that time as possible in the care of the sick. Nor must we be forced to obtain more office help, which would in turn increase the cost of medical care.

The Internist

But to return to the topic of the Family Physician. Some Internists claim to be THAT individual, but how can he be, when he limits his work to adults, does no obstetrical work, does no surgery of any kind, and really is not equipped by training to serve the whole family as he ought to do to make good his claim. I know this will stir up a hornets nest, but this is to be expected. We must define what we are talking about.

The Pediatrician

Similarly, some Pediatricians also lay some claim to be the Family Physician. Truly, he cannot be this man either, by training or limitations by his Board.

The General Practitioner

This Family Physician of the future must be as much of a specialist as the surgeon, the internist, the pediatrician, the psychiatrist, and on through the list of specialties and subspecialties. In my opinion he must receive Board certification, and take his training accordingly. The medical educator must assist greatly in his development, as must those who plan the graduate training programs beyond medical school.

The American Academy of General Practice

Continued

is going through much soul searching these days, in an effort to redefine itself in light of the future. Also in my opinion there must be real exposure of the medical student to this man we presently call the General Practitioner, or Family Physician. The only way he can achieve sufficient stature in the eyes of the public and young person making up his mind on a career is to become a bona fide specialist, with University Faculty status, and probably have Chairs of Family Practice in the Medical Schools of the Country. Many types of experiments are going to go on, all over this land, to try to develop a greater interest in this field, and to make it a meaningful specialty, attractive to enough young people, so that over the next few years a far greater number will have the desire to enter into it.

The Medical School

Our own Medical School is in trouble. It needs more money for faculty, and is actually "faculty poor." About 70-80% of our University of Minnesota Medical School budget comes from Federal money in one form or another, and these research people and others who are not paid strictly as faculty members must be used to fill the gaps in the full time teaching staff.

Increase Enrollment

I am fully aware of the need for more physicians especially in the private practice sector. These numbers have been dwindling over the last 20 years, and I'm now talking about not only Family Physicians but many other segments of the private sector. Higher percentages are going into full time research, government service or industry, actually leaving fewer doctors per 1000 of population than we had a few years ago. Our own Medical School must expand as soon as possible to 200 students, then eventually to 250 as more facilities and teachers are available.

A Second Medical School

I'm in favor of a second medical school such as has been proposed for St. Paul, but only if it is affiliated with a major university and this could be done. If it would not so affiliate, it would be a weaker school at the very outset, and we might as well plan properly for this

second school or not at all. I'm not even sure if the State of Minnesota can afford two schools, and have their major support come from tax funds, but this may not be the plan for the second school. We certainly need to encourage our legislators to put more money into the one excellent school of medicine we have at the University of Minnesota and then see if we can afford to support a second school in a major fashion.

The Role of Private Hospitals and Practicing Physicians

The University of Minnesota Medical School is running low on patients and needs our help. Admittedly it is easier for those of us who practice outside the Twin City area to talk, and I can just hear my metropolitan colleagues saying to me, "If you lived and worked here, you'd whistle a different tune". Maybe so.

Referral of Private Patients

But something has to give, and it must of necessity start in the metropolitan area, but certainly should be shared by all of us, no matter where we practice in the state. I am talking now about the problem of seeing that the patient shortage for clinical work at the Medical School be unselfishly solved by deliberately developing as rapidly as possible both an adequate outpatient clinic, and in-hospital referral of surgical and medical patients for work by all the specialties represented therein. As I have said, the day of the so-called charity patient is about gone, hence we have no choice but to face that fact squarely, and work out a system to accomplish just this with the use of private patients. The Hennepin and Ramsey County Medical Societies together with the Twin Cities Hospitals are going to have to cooperate in this venture and lead the way toward its solution. There has always been a certain amount of friction between the Medical School Faculty and the practicing physician, but much of this is going to have to be buried and some real statesmanship shown on the parts of all those involved in order to solve the multitude of problems that lie ahead. We are all physicians, and, as the old saw goes, "if we don't hang together, we'll hang separately".

Conclusions

I don't pretend to have all the answers to these many questions, but do believe that there are reasonable answers to be found, without losing any more of our rights as private practicing physicians than we have already lost. The experiments being developed in Oklahoma and elsewhere will be watched with great interest. However, we don't need to wait for anyone else to develop an "ideal plan" because there may be no such thing.

Each medical school must develop its own plan, so we will hopefully wind-up with about 90 plans, each one unique unto itself because of its own necessarily different structure. But we must quit paying nothing but lip service to the idea of increasing the actual numbers of Family Physicians. While medical education may not have wittingly assisted in the great diversion of students into fields other than Family Practice, although each department must of necessity develop its own little empire, they must now actively plan and carry out some method such as I have suggested which will attract young people into this new specialty in ever increasing numbers until a better balance is reached. How long will this take? This cannot be answered very well until we see how successful the several medical schools are in the development of these new departments. Certainly it will be a minimum of four to eight years, even if a Chair of Family Practice could be started this year at the University of Minnesota, and we hope it will be.

Much has to be worked out in terms of further definition of this MEDICAL MAN of the future, the FAMILY PHYSICIAN. What shall his curriculum be? Shall the basic 4 year course remain

the same for all students, as it is now, or shall specialization begin with the very first year, or the second or the third? Much debate and thought must be given to this matter—AND NOW. Time is short, really, and no more must be wasted in debate about the necessity for such a program.

I hope we are all agreed on this. That these Family Doctors are needed now, so let's get on with it in any way that we can. Errors have been made and will continue to be made in finding the best method, but if the cooperation between private practice and University Faculty is developed to a greater degree, the job can be done without any question. We have many interested individuals and groups, eager to get started. One good beginning would be to have the University of Minnesota Medical Faculty put on a drive within their own numbers to join organized medicine. Too many of our faculty people have remained aloof from membership in Ramsey or Hennepin County Medical Societies as well as the Minnesota State Medical Association and AMA, and it has been a major deterrent, in my opinion, to closer ties and cooperation between the faculty and the private sector of medicine in our state.

Petty attitudes, jealousies and the like, which I have seen exhibited by both faculty and private medicine alike must be minimized. It cannot be stamped out entirely and have all be "sweetness and light", unfortunately. We have a remarkable opportunity here in Minnesota to lead the nation in this endeavor as we have done in times past in other efforts, so let us all accept this challenge and create a brighter future for medicine and the people we serve.

Charles G. Sheppard, M.D.
President

William III (1650-1702)

He was sickly and was continually worried about his health. He sometimes wrote to foreign physicians under an assumed name in order thus to obtain an unprejudiced opinion of his illness. The opinions were always unfavorable. He suffered with malaria and probably had tuberculosis, for he was for a long time tormented with a racking cough and at autopsy the left lung was found diseased. He also suffered with boils, and to treat them he dusted his skin with a mixture of flour and dried and powdered eyes of crabs. His death was hastened by a fall from his horse, from which he suffered a fracture of the right collar bone.*

*Haggard, Howard W., M.D.: *Devils, Drugs, and Doctors*, Blue Ribbon Books, Inc., New York City, 1929, p. 221.



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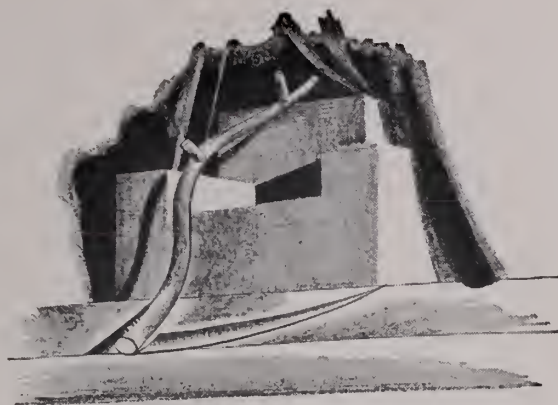
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In Memoriam

Men fear death, as if unquestionably the greatest evil, and yet no man knows that it may not be the greatest good. — W. Mitford

CARL G. SWENDSEEN, M.D.

Dr. Carl G. Swendseen, 72, Minneapolis eye, ear, nose and throat specialist, died April 9 in Pompano Beach, Florida. Born in St. James, Dr. Swendseen was a graduate of the University of Minnesota Medical School. He moved to Pompano Beach ten years ago.

He was a member of Khurum Lodge No. 112, AF & AM, Scottish Rite, Zuhrah Temple, the Swedish Hospital staff, Hennepin County Medical Society, American College of Surgeons and the American Medical Association. He was an associate member of the Minnesota State Medical Association.

He is survived by his wife and two sons.

ARTHUR C. KERKHOF, M.D.

Dr. Arthur C. Kerkhof, 63, Minneapolis heart specialist, died May 5, while attending a staff meeting at St. Barnabas Hospital. Born in Minneapolis, Dr. Kerkhof received his medical degree at the University of Minnesota.

Medical director for the Minneapolis Star and Tribune and Federal Cartridge Corporation, he was also a member of the National Board of Directors of the American Heart Association and chairman of the American Therapeutic Committee on Education. He was a past president of the Association of Minnesota Internists and the Minnesota Heart Association.

In addition, he was a member of the Hennepin County Medical Society, American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, a daughter and two sons.

CHRISTIAN A. FJELDSTAD, M.D.

Dr. Christian A. Fjeldstad, 83, Minneapolis ear, eyes and nose specialist, died April 21. He had practiced ophthalmology in Minneapolis for forty-seven years.

A former staff member of the University of Minnesota Hospitals and Fairview Hospital, Dr. Fjeldstad was a

member of the Hennepin County Medical Society and the American Medical Association. He was a 50 Club and Life Member of the Minnesota State Medical Association. In 1962 he received the Distinguished Service Award from Luther College, Decorah, Iowa.

He is survived by his wife, a daughter and a son.

HAROLD J. ROTHSCHILD, M.D.

Dr. Harold J. Rothschild, 83, St. Paul ear, eyes and nose specialist, died April 20. Born in St. Paul, Dr. Rothschild practiced ophthalmology in St. Paul for fifty-six years. He received his medical degree from the University of Minnesota Medical School.

A member of the staff at St. Josephs Hospital, Children's Hospital and St. John's Hospital, Dr. Rothschild was a member of the Minnesota Academy of Ophthalmology and Otolaryngology, American Academy of Ophthalmology and Otolaryngology, Ramsey County Medical Society and the American Medical Association. He was a Life and 50 Club Member of the Minnesota State Medical Association.

He is survived by his wife.

FRANK J. ELIAS, M.D.

Dr. Frank J. Elias, 74, a physician in Duluth for half a century, died April 7, after a long illness. Before his retirement because of ill health five years ago, he had been associated as a partner in the Morgan Park Medical Center. A native of Racine, Wisconsin, and a graduate of the Marquette University Medical School, Dr. Elias came to Duluth to intern at St. Mary's Hospital and later was associated in practice with Dr. W. H. Magie.

He was a past president of the Minnesota State Medical Association, a past president of the St. Louis County Medical Society, a Minneapolis delegate to the American Medical Association, served as chief of staff of the St. Mary's Hospital, past president of the Interurban Medical Society of Duluth-Superior, and had been

Continued

IN MEMORIAM

a member of the state advisory board council on hospital construction from its inception. In 1954 he was given the Distinguished Service Medal of the Minnesota State Medical Association.

He was a fellow of the American College of Surgeons and a 50 Club and Life Member of the Minnesota State Medical Association.

Dr. Elias is survived by his wife, a daughter and a son.

WILLIAM THOMAS WALSH, M.D.

Dr. William T. Walsh, 56, Minneapolis physician, died April 6. He was a graduate of the University of Minnesota Medical School and was chief of staff at St. Barnabas Hospital in 1956.

Born in Minneapolis, Dr. Walsh was a member of the Hennepin County Medical Society, Minnesota State Medical Association and the American Medical Association.

He is survived by his wife.

JOHN G. W. HAVENS, M.D.

Dr. John G. W. Havens, 90, former Austin EENT specialist, died May 4, at the home of his niece in Minneapolis. Dr. Havens practiced medicine more than fifty years, most of this time in Austin, where he also was well known as a Dahlia grower, an astronomer and portrait sketcher. One day before his 87th birthday, Dr. Havens closed his office in Austin.

Born in Burrsville, New Jersey, he received his medical degree from the University of Pennsylvania Medical School and in 1907 left Philadelphia to set up an office in Cloquet, Minnesota. He remained in Cloquet until shortly after the devastating forest fire which consumed much of that area. From Cloquet he moved to Owatonna, and in 1920 moved to Austin.

He was a member of the Mower County Medical Society and the American Medical Association and a 50 Club and Life Member of the Minnesota State Medical Association.

He is survived by his niece, Mrs. H. G. Sirk.

JOHN deJ. PEMBERTON, M.D.

Dr. John deJ. Pemberton, 80, a pioneer in goiter surgery at the Mayo Clinic, died May 18. Born in Wadesboro, North Carolina, Dr. Pemberton received his medical degree at the University of Pennsylvania.

He became a resident of the Clinic in 1913, ten years after the institution was founded. He retired in 1952 after thirty-four years as head of a surgery section. Dr. Pemberton was president of the Clinic staff from 1942 to 1945.

Dr. Pemberton was a fellow in the American College of Surgeons and a member of the American Medical

Association, the American Surgical Association, the Southern Surgical Association, the Southern Medical Association, the Societe Internationale de Chirurgie, the Society of Clinical Surgery, the Alumni Association of the Mayo Foundation, the Zumbro Medical Society and a 50 Club and Associate Member of the Minnesota State Medical Association.

He is survived by his wife, four sons and a daughter.

BENJAMIN I. DERAUF, M.D.

Dr. Benjamin I. Derauf, chief surgeon for the Northern Pacific Hospital, St. Paul, for forty-three years, died May 21, at the age of 73. He retired as chief surgeon of the hospital in 1962.

Born in Creston, Iowa, and a graduate of the University of Iowa Medical School, Dr. Derauf became associated with the Northern Pacific Hospital in 1925.

He was a member of the Ramsey County Medical Society, the American College of Surgeons, St. Paul Surgical Society, Minnesota Surgical Society, Minnesota Occupational Medicine Association, American Medical Association and a Life Member of the Minnesota State Medical Association.

He is survived by his wife, one daughter and three sons, one of whom is Dr. Donald E. Derauf of St. Paul.

THOMAS J. DEVEREAUX, M.D.

Dr. Thomas J. Devereaux, 77, Wayzata surgeon, died April 30. Born in Elma, Iowa, and graduated from the Rush Medical School in 1915, Dr. Devereaux immediately went into the medical corps of the United States Army. Upon his release from the Army, Dr. Devereaux came to Wayzata to practice medicine.

He was a member of the medical staff of the Eitel Hospital, the Hennepin County Medical Society and the American Medical Association. He was a 50 Club Member of the Minnesota State Medical Association.

He is survived by his daughter.

EDWARD DYER ANDERSON, M.D.

Dr. Edward Dyer Anderson, 75, a former president of the Hennepin County Medical Society, died May 29, in Rougemont, Switzerland.

Born in Duluth, Dr. Anderson graduated from the East High School in Minneapolis and the University of Minnesota Medical School. He served as assistant and associate professor of pediatrics at the University from 1918 to 1954. He retired from practice that year due to poor health and moved to Gstaad, Switzerland.

He was a member of the American Medical Association, the American Academy of Pediatrics and the Northwest Pediatric Society, and an Associate Member of the Minnesota State Medical Association.

He is survived by his wife and four sons.

The Physician's Workshop

The Operative Cystic Duct Cholangiogram

A Simplified Method of Securing the Catheter During Dye Injection

AT TIMES the operative cystic duct cholangiogram forms an integral and important part in the relief of biliary tract disease. This paper deals with a rapid and simplified method of anchoring the cystic duct catheter in place in cases where securing it easily and quickly by means of a ligature is hampered by difficult exposure.

Case Report

A 54-year-old male was admitted to the Veterans Administration Hospital for routine cholecystectomy, following multiple bouts of right upper quadrant pain. Oral cholecystogram had demonstrated multiple small stones in the gallbladder. Operation confirmed this and also revealed a large cystic duct, and it was elected to perform a cystic duct cholangiogram. Before removing the gallbladder the cystic duct was ligated distally and a small opening was made in one wall proximal to the ligature. A polyethylene catheter was next inserted through this opening into the common bile duct. Three small Cushing silver clips were then placed on the cystic duct overlying the polyethylene catheter, both securing it in place and preventing regurgitation and loss of dye into the peritoneal cavity during performance of the cholangiogram. A suture was then sewn through the skin of the abdominal wall and tied around the catheter to further aid in stabilization (Figure 1).

Review of the operative cholangiogram (Figure 2) failed to reveal any abnormalities. The silver clips were then easily removed, and the cystic duct ligated, the gallbladder having been extirpated while the films were being developed. The patient went on to recover uneventfully.

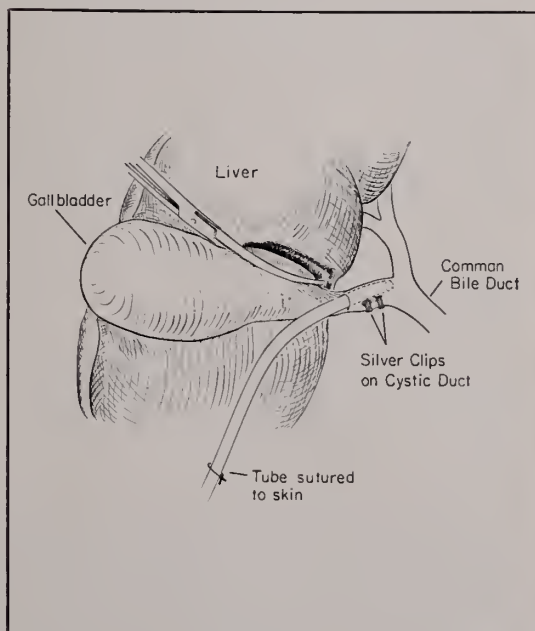


Figure 1



Figure 2

Fig. 1 — Drawing showing the use of Cushing silver clips during an operative cholangiogram. After the cystic duct is ligated, an incision is made in one wall proximal to the tie and the catheter for dye injection inserted into the common bile duct. Cushing silver clips are then applied to the cystic duct to anchor the catheter in place and prevent regurgitation of dye into the peritoneal cavity during injection. As an added precaution to prevent accidental removal of the catheter, an anchoring stitch is placed about it at the skin margin.

Fig. 2 — Photograph of the normal operative cholangiogram of patient, age 54, during routine cholecystectomy (see text for details). Cushing silver clips (arrow) were used to secure the catheter in place during performance of the dye study.

Continued

Comment

Technical difficulty in performing an operative cholangiogram or the unwillingness to prolong a short operation has allowed the surgeon at times to omit this often vital procedure during cholecystectomy.¹

The method just described was developed after considerable time had been wasted during a previous operative procedure while trying to perform an indicated cholangiogram. This resulted from repeated loss of exposure each time an attempt was made to fasten the cholangiogram catheter in place by means of a suture looped and tied both around it and the cystic duct. This use of Cushing silver clips, besides the speed with which they may be applied, has the advantage of utilizing only one hand of the operating surgeon, thereby leaving his other hand and both those of his assistant free to maintain good visualization of the operative field.

While other rapid methods of performing cholangiograms have been devised to offset difficulties of exposure and operating time loss, such as direct puncture of the common bile duct with injection of dye through a 22-gauge needle² or by the development of needles of more sophisticated design,³ we feel that when the cystic duct route is used, the method described offers a safe and easy method of maintaining the biliary tract catheter in place.

A simplified method utilizing Cushing silver clips to anchor the catheter introduced through the cystic duct in order to perform an operative cholangiogram has been described.

Raymond C. Bonnabeau, Jr., M.D.*

Martin L. Beard, M.D.*

Minneapolis, Minnesota

*Department of Surgery, University of Minnesota Hospitals and Veterans Administration Hospital.

References

1. Maingot, R.: Abdominal Operations. Appleton-Century-Crofts, Inc., New York, p. 682.
2. McQuarrie, D.: Personal Communication.
3. Jablonoski, C.: A Method of Operative Cholangiography. Surg Gynec Obstet 122:1087, 1966.

The Bridge

Memoirs of a Lady Ambulance Surgeon

During my time at the hospital, the Williamburg Bridge was being built and we lived in the shadow of this great structure, a marvel of engineering in those days. To the average person that is probably what it means. For me, however, it will always spell a great company of living men out in the open and bravely battling the elements, using their flaming forges as they tossed around the red-hot rivets with a breath-taking precision. I used to watch them going from girder to girder, sure-footed, debonair and oblivious of the terrible distances below them. Their jokes and songs rang out on the frosty air, as they built for the use and comfort of coming generations. And then there would be a hurry call and I would find myself passed along like a chip in the wind by the blue coats, who would take charge, when some of those mighty girders missed connections and came crashing down, carrying some splendid fellows with them. As I tried to reassemble the poor mangled forms I had ready always that blessed hypodermic of morphine to assuage their agony. No, that bridge will remain for me always a living, vibrant memorial to the unsung heroes who built it.

—Emily Barringer, M.D.
Bowery to Bellevue, 1950.

Special Article

A Demonstration of Anti-Inflammatory Effect of Indomethacin

NEW THERAPY in the rheumatic diseases is always suspect. A major problem in evaluating anti-rheumatic drugs is the lack of easily reproducible objective criteria by which to measure their effects. Indomethacin is a new drug recently released as an anti-inflammatory agent for the treatment of rheumatic diseases. Experimental studies in animals have demonstrated an anti-inflammatory action, and numerous clinical reports have indicated the usefulness of indomethacin in the therapy of arthritic disorders. Yet few of the human studies present clear objective evidence of an anti-inflammatory action of indomethacin. Smyth¹, in a carefully controlled study using some of the best available objective measurements of rheumatic activity, has presented data supporting the efficacy of this drug.

The authors recently had an opportunity to observe an objective, easily monitored manifestation of rheumatoid arthritis which responded dramatically on four occasions to indomethacin. The patient is a 48-year-old white female with classical rheumatoid arthritis under treatment at the Kenny Institute. In the past she suffered from a severe episcleritis* of the right eye, which had been suppressed by her maintenance dosage of 15 mgm. of prednisone daily. During the course of steroid reduction to 4 mg. prednisone daily, a flareup of the episcleritis occurred along with a generalized exacerbation of her arthritis. Indomethacin was administered starting 9/1/65 in a dose of 100 mg. a day with prompt suppression of the episcleritis and reduction of the articular manifestations.

Following discontinuation of indomethacin on 10/11/65 the episcleritis recurred and her arthritis became worse despite continuing the same 4 mg. daily dose of prednisone. The episcleritis was only partially controlled by the daily local use of corticosteroids. On 12/28/65 the indomethacin was resumed with improvement in the articular symptoms and clearing of the episcleritis. On 1/10/66 the drug was discontinued due to a gastrointestinal upset. The episcleritis flared

*See Test Your Word Score Page 1097.



Fig. 1 — Episcleritis right eye 48 hours after stopping indomethacin. Note blepharospasm.



Fig. 2 — Absent episcleritis 6 days after restarting indomethacin.

Continued

SPECIAL ARTICLE

promptly, and on 1/13/66 the indomethacin was resumed with improvement of the episcleritis within 24 hours. As a test the drug was discontinued a third time on 1/18/66 and resumed on 1/21/66 when it was apparent that the episcleritis became worse with interruption of indomethacin and was promptly suppressed on resumption of the drug. An ophthalmologist was called in during this trial to verify the eye changes while on and off indomethacin. A last trial, accompanied by photographic documentation (Figures 1 and 2), was made when the drug was stopped on 2/27/66 with the episcleritis appearing on 2/28/66 and becoming moderately severe by 3/1/66 when the drug was resumed. Again, improvement was noted within 24 hours and suppression was maximal after four days.

Summary

Objective clinical evidence of an anti-inflammatory effect of indomethacin is presented in a patient with classical rheumatoid arthritis and episcleritis, who on four separate occasions developed a flare in her episcleritis which was promptly suppressed by indomethacin.

Robert L. Swezey, M.D.*

Paul J. Bilka, M.D.**

Minneapolis, Minnesota

*Department of Physical Medicine and Rehabilitation, University of Minnesota School of Medicine.

**Department of Medicine, University of Minnesota School of Medicine.

Reference

1. Smyth, Charley J.: Indomethacin in Rheumatoid Arthritis. A Comparative Objective Evaluation with Adrenocorticosteroids, *Arthritis Rheum* 8:921, 1965.

Biological publication now costs almost six cents a word. But more than money is at stake. Economy of communication and reading time is the major concern. Economy of words also yields clarity. *I found* costs less than half as much as *it was discovered*, and it identifies the discoverer immediately. When *experiments were conducted*, the reader cannot tell whether you or your predecessors conducted them. If you use *I* or *We* . . . you easily avoid the passive voice, at least in that one sentence. *I* may embarrass *the writer*, but it takes less than one-tenth the space.

Committee on Form and Style
Style Manual of Biological Journals

Part of the secret of success in life is to eat what you like and let the food fight it out inside.

—Mark Twain

No cigar smoker ever committed suicide.

—William Maginn

Tuberculosis

A Revised Tuberculosis Control Program For Minnesota

To speed the control and eventual eradication of tuberculosis in Minnesota, the following recommendations are offered:

I. *Facilities and Personnel*

1. A physician with training in public health and with adequate experience in the control of tuberculosis should continue to be employed by the Minnesota Department of Health as a Tuberculosis Control Officer to coordinate and carry out the anti-tuberculosis program for the entire state. The value of this has already been demonstrated.

2. The additional personnel and facilities necessary for implementation of the tuberculosis control program should be provided by the Minnesota Department of Health to assist physicians and county nurses in the follow-up and management of tuberculous patients and to assist in obtaining epidemiologic data concerning tuberculosis.

3. The public health nursing staff in the counties or areas should be commensurate with the local tuberculosis problem and adequate to conduct a vigorous anti-tuberculosis program.

4. The eight district offices of the Minnesota Department of Health should assume greater responsibility for local tuberculosis control, and each district should maintain a case register.

5. The Minnesota Department of Health should continue, within its capacities, to provide laboratory services for the sensitivity testing of tubercle bacilli when requested by the physician.

6. Mortality from tuberculosis should be reviewed by the Tuberculosis Control Officer of the Minnesota Department of Health.

7. There is need for continued coordination of the entire anti-tuberculosis program, and the logical center for this effort is the office of the Tuberculosis Control Officer of the State Department of Health. The excellent work being done by state and local health departments, school health programs, sanatoria, hospitals, practitioners, the Livestock Sanitary Board, and the voluntary health agencies could be made even more effective by better coordination of effort without reducing the value or prestige of any group.

II. *Case Finding*

1. We should strive by every means possible to encourage the private physician to utilize tuberculin tests and chest x-rays routinely in the care of the apparently healthy as well as of the ill patient, and to use consultation.

2. Tuberculin surveys:

a. Local physicians in cooperation with the local health departments and the Christmas Seal organization should be encouraged to carry out tuberculin testing programs in the public and parochial schools of their areas.

b. Approval is given to the school tuberculin testing program approved in December, 1965, by the Minnesota Tuberculosis and Health Association, based on the NTA Task Force Report. It is stipulated further that this program be regarded as the "minimum standard."

The minimum program for school tuberculin testing shall include school enrollees, transfers at any level, seventh graders and eleventh graders.

If the tuberculin reaction rate is above 1 per cent in any school district, the need for a more extensive testing program is indicated.

A "positive reactor" shall be considered to be one with a reading of 10 mm. or more of induration for extensive follow-up considerations and for the purpose of computing the 1% reaction rate mentioned above.

Reactors with between 5 and 9 mm. of induration should have reaction recorded as doubtful and should be retested within one year. The recommended doses are 5 tuberculin units or 0.1 cc. of 1:1000 O.T.

c. All positive reactors to tuberculin found in school tuberculin surveys should have chest x-ray examinations, with thorough investigation of contacts.

3. All school teachers and school employees are required by law to show freedom from active tuberculosis as evidenced by an annual chest x-ray examination or by presenting evidence of a negative tuberculin reaction within the preceding year.

4. All colleges, trade schools and similar institutions should be encouraged to require a stu-

Continued

dent to have a tuberculin test, and a chest x-ray if tuberculin positive, on admittance to the school.

5. The following groups having an increased incidence of tuberculosis should have chest x-rays and appropriate investigation of any abnormal findings:

- a. Persons admitted to jails and workhouses
- b. Persons admitted to Salvation Army shelters and similar facilities
- c. All food handlers, annually
- d. Persons admitted to nursing homes, rest homes and homes for the aged
- e. All persons more than 15 years of age who are admitted to hospitals or hospital outpatient clinics

f. Contacts of local cases

6. Mobile Unit Chest X-ray Surveys:

a. Chest x-ray mobile units, now available on a statewide basis, should be continued by Christmas seal organizations.

b. Mobile unit chest x-ray surveys should be conducted annually among those having an increased incidence of tuberculosis, such as migrant workers, skid-row inhabitants and residents of congested population centers.

7. Pathologists, private physicians and clinical laboratories should be encouraged to cooperate in reporting all newly discovered cases of tuberculosis.

III. *Treatment of Active Tuberculosis*

1. Adequate diagnostic and treatment facilities should be available to all patients with tuberculosis.

2. Management of tuberculosis by chemotherapy should be recognized as a public health as well as a purely medical problem and responsibility.

3. Treatment of the patient with active tuberculosis must be under continuous medical supervision and should be instituted within a hospital, preferably one specializing in tuberculosis, and hospitalization should continue until the disease is no longer communicable. At present, this is the best means of instituting adequate therapy, of educating the patient about his illness, and of helping him adjust to it. Hospitalization is particularly important to protect the patient's family and the public from infection.

4. The decline in the number of hospitalized tuberculous patients makes it economically diffi-

cult to maintain most of our sanatoria. Therefore, patients should be centralized in hospitals or sanatoria where it is economically feasible, with due regard for the maintenance of high standards of medical care. Sanatorium or hospital facilities must be maintained as long as the need exists. Private and public general hospitals should be encouraged to accept patients with active tuberculosis, but only if satisfactory isolation can be maintained and if the treatment of tuberculosis can be supervised by a physician experienced in the management of the disease.

5. All patients are discharged from sanatoria or hospitals before treatment is completed, and an occasional selected patient is treated without hospitalization. When the patient is referred to the care of another physician, the tuberculosis specialist should make specific recommendations for continued care and follow-up and should maintain close cooperation with patient and physician thereafter.

IV. *Prevention and Prophylaxis*

1. Vaccination with BCG should be considered only in instances in which a non-reactor to tuberculin is going to experience unusual exposure to tubercle bacilli.

2. The Infectious Disease Committee (or other appropriate committee) of private or public general hospitals, together with hospital administrators, should establish and supervise a standardized technic for room isolation of patients with known or suspected active tuberculosis.

3. The Infectious Disease Committee and administrators of all hospitals should organize a tuberculosis prevention program for hospital personnel.

4. The successful program of tuberculosis surveillance among cattle and livestock, established and maintained by the Minnesota State Livestock Sanitary Board, should be continued by that Board.

5. Prophylactic chemotherapy with isoniazid is recommended for the following:

- a. Children up to two years of age who have been exposed to a patient with open tuberculosis
- b. Tuberculin reactors in the preschool age group
- c. Adults and children with known or probable recent tuberculin conversion
- d. Tuberculin reactors under long term steroid therapy

e. Patients with inactive tuberculosis who have never had adequate chemotherapy and are suffering from conditions known to cause increased susceptibility to reactivation, such as diabetes, gastrectomy, silicosis, acute pneumonia, severe trauma or alcoholism, and certain debilitating and terminal diseases such as lung cancer.

V. *Follow-Up and Rehabilitation*

1. The physician in charge of the patient with active tuberculosis must not only supervise treatment, which is necessarily prolonged, but also impress on the patient's mind the need for follow-up treatment and examinations, for the rest of the patient's life. The Health Department, through the Tuberculosis Control Officer, should follow up this patient's illness indefinitely.

2. Follow-up of contacts of patients with active tuberculosis is essential, and private physicians and public health authorities must both assume this responsibility and cooperate fully.

3. In each case of tuberculosis, the goal is: prevention of spread of the disease to others; cure of the patient with tuberculosis with a minimum of inconvenience, expense and disability; and complete restoration to an active productive life. Without rehabilitation, treatment is only partly successful.

VI. *Education, Research and Coordination*

1. Education of the public, physicians and other professional groups in the basic principles of modern tuberculosis control should be persistent and intensive.

2. The private physician plays an essential role in the treatment of tuberculosis. More information regarding control and therapy must be made available to him.

3. Lay and professional organizations and federal and state government agencies should foster and finance scientific research on matters of current importance to tuberculosis control, with special reference to problems in Minnesota.

VII. *Legislation*

1. The legislative committees of the Minnesota Thoracic Society and the Minnesota Tuberculosis and Health Association should work with the State Board of Health and the appropriate committee of the Minnesota State Medical Association for the purpose of proposing legislation regarding tuberculosis care and control to be presented to the Minnesota state legislature.

2. The "means test" should be abolished in Minnesota for all patients being treated for tuberculosis in tax-supported institutions, and all patients in these institutions should be given free medical and hospital care regardless of their ability to pay.

3. Budgetary requests of the Minnesota Department of Public Welfare and the Minnesota Department of Health for improvement of the tuberculosis program in Minnesota should be approved by the state legislature, or if significant changes are considered, the groups sponsoring this joint statement should be consulted before legislative action is undertaken.

Joint statement by the:

Minnesota Chapter of the American College of Chest Physicians
Minnesota League for Nursing
Minnesota Nurses Association
Minnesota State Department of Health
Minnesota State Livestock Sanitary Board
Minnesota State Medical Association
Minnesota Thoracic Society
Minnesota Tuberculosis and Health Association
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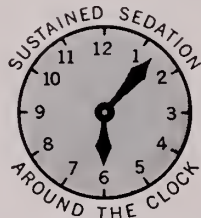
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INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X-ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE—289; 496 Lowry Medical Arts Building; St. Paul, 55102.

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LOCUM TENENS wanted for general practice from now through summer 1967. Write: MINNESOTA MEDICINE—377, 496 Lowry Medical Arts Building, St. Paul 55102.

GENERAL PRACTITIONER wanted to join well established practitioner. Located 65 miles north of Minneapolis-St. Paul area. Population over 3,000. Hospital in town. Good schools, churches, and fine fishing and recreational area. Contact: A. C. Peterson, M.D., 200 E. Forest St., Mora, Minnesota 55051.

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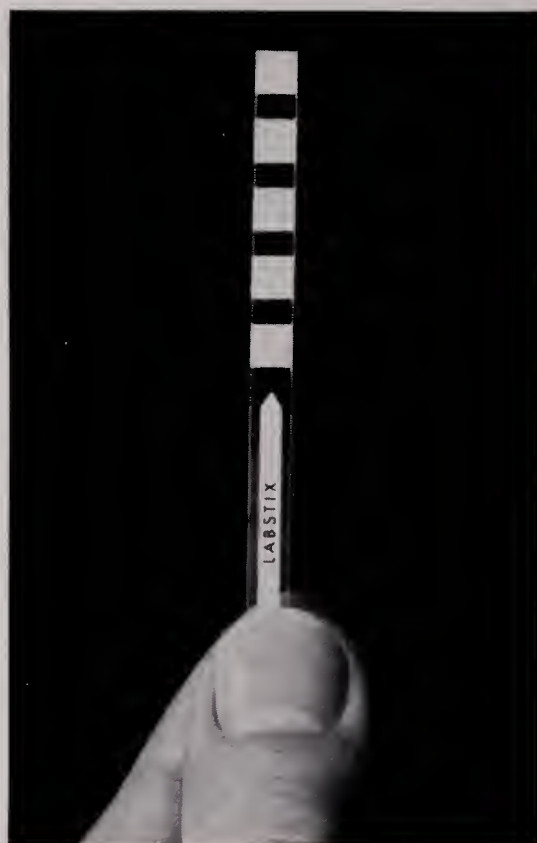
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FOR SALE: Keleket X-ray unit 100 MA. — full wave rectification — table has buckey — four sizes high speed cassettes — contact: Earl Helwig, M.D., 2234 Dunedin Avenue, Duluth 55803.

GENERAL PRACTICE associate wanted for young three man group in populous growing area located 30 minutes south of the Twin Cities. Spacious three year old clinic with new accredited hospital and nursing home in same town. Salary and terms open. Contact River's Edge Medical Clinic, Farmington, Minnesota. Telephone 463-7181.

CLINICAL DIRECTOR in accredited progressive 2600 bed mental hospital with fully approved residency training program. Ideal living in active community in the heart of Michigan's Water Winter Wonderland vacation area. Requires Psychiatric Board Certification. Salary \$20,984 to \$25,891. Furnished housing available, unparalleled fringe benefits. Contact: M. Duane Sommerness, M.D., Supt., Traverse City State Hospital, Traverse City, Michigan 49684.

GENERAL PRACTITIONER: To engage exclusively in outpatient work on a part-time basis. Regular hours will be arranged to suit convenience of applicant. No night call or weekend work. Contact: D. W. Ferguson, M.D., Veterans Administration Outpatient Clinic, Fort Snelling, St. Paul, Minnesota 55111. Phone: 721-2955, Ext. 256.



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INTERNIST, PEDIATRICIAN and Ob-gynecologist wanted to join two general surgeons in a rapidly growing practice. Attractive town of 3,000 on large lake 30 miles west of Twin Cities. New 55-bed JCAH hospital with plans for major expansion. Five other physicians in town. No Ob-Gyn., internist, or pediatrician in area. Medical community serves in an area with population of 20-25,000. Planning to expand into partnership multi-specialty clinic. Call or write: Savaryn Clinic, Waconia, Minn. 55387. Telephone: 442-2137.

WANTED: General practitioner, to join two G.P.'s well established in north central Minnesota community, 2200 pop., 65 miles from Twin Cities. Excellent office space with lab and X-ray, just opened new hospital, all facilities. Assistantship or partnership. Considerable surgery and obstetrics. Hunting, fishing, golf club. Great opening for interested G.P. **WRITE MINNESOTA MEDICINE—381, 496 Lowry Medical Arts Building, St. Paul, 55102.**

GENERAL PRACTITIONER OR PEDIATRICIAN WANTED to join general practitioners affiliated with group in neighboring town in northeastern Minnesota. Basically medicine and pediatrics on outpatient basis; Obstetrical and hospital practice optional. Eight days off each month in any mutually agreeable manner plus liberal vacation and study leave. Present physician devotes part of days off in medical missionary work. Starting guarantee \$18,000 to \$26,000 after 4 years. No investment; full partnership after six months. Age no barrier. Contact: Richard Rowe, M.D., Silver Bay, Minnesota 55614.

Opportunity for career in occupational medicine. Opening for full-time plant physician Southern Minnesota major meat packing company. Excellently staffed and equipped in-plant Medical Department. Regular hours, excellent benefits, salary open. Write T. E. Barber, M.D., Box 800, Austin, Minnesota 55912.

Wanted GP, **INTERNIST, PEDIATRICIAN.** Position with six man medical group associated with company prepayment plan in northeastern Minnesota. Well equipped 38 bed accredited hospital next door to clinic, and two large hospitals in community 25 miles away. Internist and pediatrician to work as consultants in clinic and hospital. Ideal for physician desiring small community practice. Full partnership after six months; rotating call schedule; four weeks vacation, sick and study leave; and retirement plan. Group working toward additional periodic extended study or vacation leaves. Age no barrier. Starting guarantee 18 to \$20,000 with increases to 26 to \$28,000 in four years. Contact: Harold B. Leppink, M.D., Community Clinic, Two Harbors, Minnesota 55616.

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Febrile reactions to influenza vaccine are reported to be markedly reduced after the use of a new purified influenza vaccine reported at the American Society for Microbiology on 2 May, 1967. (Parke-Davis Company).

Atabrine (quinacrine) has been given intrapleurally and intraperitoneally in the treatment of neoplastic effusions and favorable results are reported in the Annals of Internal Medicine (66:249, 1967). Fever and pleuritic pain were noted after intrapleural injection, but responses were obtained in patients who previously failed to benefit from other agents. This use of Atabrine is experimental and has not yet been cleared by the FDA. (Winthrop Laboratories).

Physician attention is called to a new dosage form of sodium cephalothin, (Keflin, Lilly). The manufacturer is now making available a 4-Gm. ampoule of this antibiotic for use in those cases where particularly applicable.

Frontier Dentistry

Doctors improvised equipment for dentistry. In the Oregon bunchgrass country, Dr. Urling C. Coe regularly functioned at "tooth-pulling bees." Cowboys with toothaches rode to the host ranch from all over the range. Whiskey flasks passed from hand to hand; everybody drank and sang. Out in the yard Dr. Coe placed two kitchen chairs next to one another. His patient sat in one chair while the roistering gang crowded close. Putting his left foot on the seat of the other chair, Coe had his patient lay his head on his knee. Quickly he encircled the man's head with his left arm in a strangle hold and seized his lower jaw with his left hand. Wielding the forceps in his right hand, he grappled with the decayed tooth and pulled it out by brute force. Dr. Coe would pull out thirty to forty teeth at a session. It was a tough experience, agreed the cowboys, but not nearly so tough as having a blacksmith knock an aching tooth out with a punch and hammer.*

*Richard Dunlop, M.D.: Doctors of the American Frontier.

Culture is one thing and varnish another.—Ralph Waldo Emerson



Meetings and Announcements

The secret of a good memory is attention, and attention to a subject depends upon our interest in it. —We rarely forget that which has made an impression on our minds. — Tyrone Edwards

JULY

American Veterinary Medical Association, [E], Minneapolis, July 13-17. Act. Exec. Sec.: D. A. Price, D.V.M., American Veterinary Medical Association, 600 S. Michigan Ave., Chicago 60605.

Rocky Mountain Cancer Conference (21st Annual), Brown Palace-West Hotel, Denver, July 14-15. Info: N. Paul Isbell, M.D., Colorado Medical Society, 1809 E. 18th Ave., Denver 80218.

Southern Seminar in Obstetrics and Gynecology, Oak Grove Inn, Asheville, N. C., July 23-29. Info: William H. Robertson, M.D., 2700 10th Ave. S., Birmingham, Ala. 35205.

Symposium on the Mammalian Oviduct, Washington State University, Pullman, July 31-Aug. 4. Info: Prof. E. S. E. Hafez, Reproduction Laboratory, Washington State University, Pullman 99163.

AUGUST

American Academy of Physical Medicine & Rehabilitation, [E], Sherman House, Chicago, Aug. 17-22. Exec. Dir.: Creston C. Herold, 30 N. Michigan Ave., Chicago 60602.

International Biophysics Congress, Third, Boston, Mass., Aug. 29-Sept. 3. Info: Dr. Walter Rosenblith, Center of Communication Sciences, Room 20B-221, Massachusetts Institute of Technology, Cambridge 02139.

Wyoming State Medical Society, Jackson Lake Lodge, Moran, Aug. 26-29. Exec. Sec.: Arthur R. Abbey, P.O. Box 2266, Cheyenne 82001.

American Association of Electromyography and Electrodiagnosis, Americana Hotel, Miami Beach, Fla., Aug. 27. Info: M. K. Newman, M.D., 16861 Wyoming Ave., Detroit 48221.

American Dietetic Association (Golden Anniversary Meeting), Conrad Hilton Hotel, Chicago, Aug. 14-18. Exec. Sec.: Ruth M. Yakel, 620 N. Michigan Ave., Chicago 60611.

American Hospital Association, [E], Palmer House, Chicago, Aug. 21-24. Exec. Vice Pres.: Edwin L. Crosby, M.D., 840 N. Lake Shore Dr., Chicago 60611.

American Physiological Society (Fall Meeting), Howard University, Washington, D. C., Aug. 23-26. Exec. Sec.: Dr. Ray G. Daggs, 9650 Rockville Pike, Bethesda, Md., 20014.

American Society for Pharmacology and Experimental Therapeutics, Howard University Medical Campus, Washington, D. C., Aug. 27-31. Info: Ellsworth B. Cook, Ph.D., Exec. Sec., 9650 Rockville Pike, Bethesda, Md., 20014.

Black Hills Medical Seminar, Rapid City, S. D., Aug. 4-5. Chair.: Richard Kovarik, M.D., 728 Columbus St., Rapid City, S. D., 57701.

International Doctors in Alcoholics Anonymous, Airlie, Warrenton, Va. (Washington, D. C., suburb), Aug. 11-13. Info: Earl H. Mitchell, M.D., 3509 Dunlop St., Chevy Chase, Md., 20015.

National Medical Association, Chase Park Plaza, St. Louis, Aug. 7-10. Adminis. Sec.: Samuel C. Smith, 520 W St., N.W., Washington, D. C. 20001.

Minnesota Medicine at a Glance

Amniocentesis — Spellacy et al.

Page 1055.

This is a report of the spectrophotometric findings of amniotic fluids to which has been added maternal blood and meconium. These studies were carried out in an effort to clear up some of the false positive determinations found on amniotic fluid analyses for fetal erythroblastosis.

It was found that the addition of maternal blood to the amniotic cavity apparently does not increase the pigments used as prognostic indices in the diagnosis of erythroblastosis by amniotic fluid analysis. It was also found that by mixing meconium solution with amniotic fluid, the significant spectrophotometric peaks in the amniotic fluid were not altered. Therefore no false positive findings were created by the addition of either contaminant to the amniotic fluid.

Although this paper does not educe any startling discoveries, it does widen our knowledge in this field. This is certainly an area in which many such basic research testings must be made. In so doing, we may well find that we will gain more information regarding the status of the intrauterine infant. This knowledge, in turn, might then act as a guide in the handling of various obstetrical problems, just as it has in the handling of the erythroblastotic fetus.

Nodular Disorders — Laymon

Page 1059.

Nodular inflammatory lesions of the legs frequently pose diagnostic difficulties. Recognition of the various entities usually depends upon correlation of both morphologic and histopathologic features. Erythema nodosum, erythema induratum, nodular vasculitis, Weber-Christian disease, pernio, superficial thrombophlebitis, and periarteritis nodosa are included among the classic nodular lesions of the legs. Within the past two decades several new nodular inflammations of the lower extremities have been recognized, such as nodular fat necrosis with pancreatic diseases, subacute migratory panniculitis, necrobiosis granulomatosis, embolic nodules, and certain forms of necrotizing vasculitis such as the nodular dermal allergid. The establishment of a new syndrome must be based on a clearly recognizable clinical pattern, a microscopic picture which is sufficiently distinctive to justify its independence and a course which is characteristic enough to indicate the uselessness of a new term which implies differences in pathogenesis, prognosis, and treatment. Recognition of these entities thus aids the clinician.

Mesenteric Artery — Larson and Nydahl

Page 1067.

Acute superior mesenteric artery occlusion is a rare but nonetheless important surgical emergency, because when it is recognized early it can be completely reversed. If it is not diagnosed before bowel necrosis occurs it is usually fatal. It should be considered in all elderly patients with sudden, poorly defined abdominal pain, especially if heart disease coexists. Several presumptive x-ray signs occur, but unfortunately these develop relatively late. Prompt surgical exploration, with embolectomy and bowel resection if necessary, is essential to a successful outcome. If bowel viability is questionable at the primary operation, non-resection, followed by re-exploration twenty-four hours later, is suggested.

Solitary Myeloma of Bone — Ramos et al.

Page 1073.

One of the rarer tumors is the true solitary myeloma of bone. Most of the so-called solitary myelomatous lesions will eventually show generalized spread if they are observed long enough.

This report concerns a 43-year-old man with a solitary myeloma, or plasmacytoma, who had no recurrence or spread during a 13-year follow-up. This lytic lesion involved the third lumbar vertebra, with destruction of the pedicle and expansion of the transverse process on the right. The tumor was removed surgically, and postoperative radiation therapy was given. The lesion showed the typical histologic picture of a mature myeloma. Roentgenologic survey of the rest of the skeleton showed normal findings. Serum electrophoresis did not disclose any abnormalities in protein.

Because this patient did not have any clinical or roentgenologic signs of other myelomas during the long follow-up period, it is concluded that the lesion represents a true solitary myeloma, or plasmacytoma.

Rubella Syndrome — Staub

Page 1079.

Purpura, thrombocytopenia, intra-uterine growth retardation, hepatosplenomegaly and bone changes are the important newly described features of the congenital rubella syndrome. These have been postulated as due to an increased pathogenicity of the rubella virus. This report of careful observations of purpura, thrombocytopenia, and intra-uterine growth retardation, observed half a decade before the recent epidemics, indicates that these features occurred in the past but were not recognized as secondary to the maternal rubella.

Egyptian Remedy for the Uat Disease

If thou examinist a person with a misery in the epigastrium, he has pain in the arm, the breasts, and the belly and he is told that it is the uat disease (the green-sickness) sayest thou, accordingly, "It is caused by death which has entered the mouth and taken up its abode there." Make him a medicine of the following plants: tehua berries, poppies, peppermint, annek, the red seeds of sechet, cook it in oil and let the patient drink thereof. Lay thy hand upon him, his arm is easily extended and free of pain. Say, "This disease has passed through its proper intestinal route to the anus, I shall not repeat the medicine." Circa 850 B.C.*

*Rapport, Samuel, and Wright, Helen: Great Adventures in Medicine. The Dial Press, New York, 1952, p. 44.

The body is well, but the purse is sick.

—Erasmus

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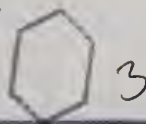
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J. J. Regan, M.D.

AUGUST, 1967

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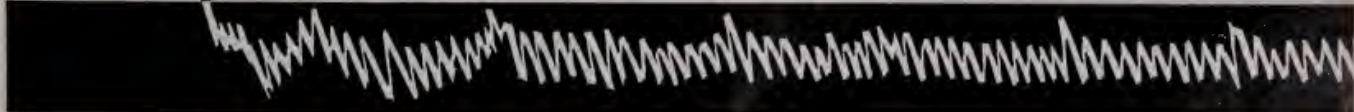
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PRESIDENT'S LETTER 1173

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William Katz, M.D. and Guilo Annessa, M.D.
Detroit, Michigan
Raymond C. Read, M.D., F.A.C.S.
Little Rock, Arkansas.....1175

Volume 50

Cardiac and Pulmonary Dyspnea—Clinical Differentiation

David E. Dines, M.D. and Thomas W. Parkin, M.D.
Rochester, Minnesota 1181

Number 8

Drugs and Doctors—Problem in the Production of Certain Behavioral Disorders

Albert B. Hagedorn, M.D. and
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References: 1. Batterman, R. C., and Grossman, A. J.: *Fed. Proc.* 14:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: *The Pharmacological Basis of Therapeutics*, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Roth, J. L. A., et al.: *Gastroenterology* 44:146, 1963. 4. Conney, A. H., and Burns, J. J.: *J. Pharmacol. Exp. Ther.* 123:340, 1960. 5. Settel, E.: *Clin. Med.* 6:1373, 1959. 6. Berman, H. H., et al.: *Dis. Nerv. Syst.* 25:430, 1964. 7. Darienzo, C.: *Ibid.*, 27:189, 1966.

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President's Letter

THIS is a plug for two very worthy efforts which some of you may not know about, but which, if you did, might stimulate your personal interest and action.

I had known about PROJECT HOPE for some time but had not known as much about it as I should until I had the opportunity to visit with Dr. Harry B. Hall of Minneapolis, an old friend and classmate of mine. Harry has been with the Good Ship HOPE on at least one trip, when it went to the Orient. He is a tremendous salesman for the project.

The other somewhat similar effort is Project VIETNAM, sponsored by the American Medical Association. I knew that Dr. Bror Pearson of Shakopee intended to join this group but didn't know all the details until the Atlantic City meeting, when Bror appeared with three other physicians on a TV program, beamed to the AMA members there at the National Meeting. Instead of a tour aboard a hospital ship, such as the HOPE is, this program is strictly for land-lubbers, and is designed to give care to the Vietnamese civilians for a similar period of time, approximately two months, I believe.

Both of these men, and I'm sure there are others available, are willing to come to one of your County Society meetings to tell you about their adventure. We gripe because of a shortage of physicians in many areas of this country, but we have no problems at all when compared to the fantastic lack of adequate medical care in Vietnam. Most of their physicians are serving with the armed forces, leaving 350 physicians to

look after the medical needs of *15 million* civilians.

There are 16 provincial hospitals for civilians, and it requires 24 to 32 physicians to keep the hospital staffs at full capacity. The types of physicians needed most are general practitioners, internists, general surgeons and orthopedists. Small numbers of physicians in other specialties are required from time to time.

These men who have served with either HOPE or in VIETNAM come home with a missionary zeal for the work that is being done. No man or woman should go into medicine without a sincere desire to be of service to mankind, but this ideal gets a bit fogged up in our land of plenty. Your value to people as their physician can be fully appreciated in an adventure of this kind, rekindling appreciation for those things which we so often take for granted here at home.

Can you spare two months of your lifetime to join either of these projects? I'm sure you would find it most rewarding.

For further details write: American Medical Association Volunteer Physicians for Vietnam, 535 North Dearborn St., Chicago, or PROJECT HOPE: P.O. Box 777, Minneapolis.

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Gastric Duplication with Pancreatic Communication

Presenting

as

Pancreatitis

WILLIAM KATZ, M.D.*
GUILLO ANNESSA, M.D.*
Detroit, Michigan

RAYMOND C. READ, M.D., F.A.C.S.*
Little Rock, Arkansas

RECURRENT INFLAMMATION of the pancreas occurs commonly in a city-hospital population. In most cases there is a history of alcoholism; less commonly, biliary tract disease. Rarely, upper abdominal trauma, previous surgery, hyperparathyroidism or drug toxicity precipitate the disorder. We have recently studied an adult negro female who presented with recurrent hyperamylasemia, outlet obstruction of the stomach, and apparent pseudocyst formation. Careful investigation over a period of six months demonstrated none of the usual causes cited above. Surgical exploration revealed a duplication cyst communicating with both the pylorus and the pancreas. There was interstitial inflammation of the duodenum and the antrum leading to partial obstruction of the gastric outlet. This unusual entity is described below.

Case Report

A 34-year-old negro female was first seen in April 1963, with a four-day history of sharp periumbilical pain radiating to the back and associated with nausea and vomiting. Her symptoms were unrelated to diet. She had been experiencing similar episodes increasingly over a period of two years.

Physical Findings

Physical examination revealed a thin woman, height 4' 11", weight 85 pounds, T 98.6, BP 96/70, R 20. She appeared acutely ill. The only positive physical findings were epigastric tenderness and muscle guarding. Laboratory studies showed a hemoglobin of 10.6 Gm%, wbc. 6,400 per cubic mm., blood amylase 936 Somogyi units (normal less than 200) and serum lipase of 3.8 units (normal less than 0.2).

Progress

She was treated non-operatively with bed rest, nasogastric suction, intravenous feeding and intramuscular antibiotics. Her condition improved so that after three days she was placed on a strict ulcer regimen with subsidence of her symptoms. However, the blood amylase and lipase levels remained elevated until the 20th and 28th hospital day, respectively. She was discharged from the hospital with a diagnosis of acute pancreatitis 32 days after admission.

While on the ulcer diet, the patient had occasional mild epigastric distress and vomiting. She was read-

*Departments of Surgery, Wayne State University Medical School, Detroit, Michigan, and the University of Arkansas Medical School, Little Rock, Arkansas.

mitted on January 2, 1934, with another exacerbation. Upper gastrointestinal series at that time suggested the diagnosis of pseudocyst of the pancreas since it revealed persistent antral deformity with some obstruction to the outlet of the stomach (Figure 1). No masses were palpable in the abdomen. Laboratory studies were unremarkable, the triolein uptake study being normal. Sweat tests to rule out cystic fibrosis were negative. A cholecystogram revealed a functioning gallbladder and a normal-sized common duct which was, however, displaced to the right.

Operative Findings

In view of the patient's continuing distress, exploratory laparotomy was performed on February 2, 1934. A 5-cm.-wide mass was found arising from the inferior border of the pyloric antrum attached to the head of the pancreas (Figure 2). The greater omentum was separated and the pylorus opened through an anterior pylorotomy. A stomal opening was found in the mucosa of the pyloric area on its inferior posterior surface (Figure 3). A probe passed into this opening entered an apparent duplication measuring 3×3 cm. The neck of this cyst had perforated interstitially into the wall of the antrum and also into the duodenal wall for a distance of some two inches above and below the pylorus (Figure 4). The mucosa of the duodenum and antrum was thickened and raised into the lumen. The cyst wall was lined with epithelium demonstrated on frozen section to be gastric, containing both mucus-secreting and chief cells (Figure 5). The external wall of the cyst was continuous with the seromuscularis of the gastric antrum and was attached at its base to a lobular extension of the pancreas from which clear fluid could be expressed from multiple lumina into the duplication.

The neck of the cyst was excised and the pyloroplasty closed so as to incorporate the duplication (Figure 6). It was considered unwise to separate the lobules of the pancreas from their firm attachment to the posterior wall of the cyst for fear of damaging the main pancreatic duct. A vagotomy was also performed. The patient made an uneventful recovery and three years later feels well and has gained 53 pounds (Figure 7).

Discussion

Duplication cysts are defined by Gross and



Fig. 1—This is a preoperative barium study showing gastric retention with extrinsic compression of the antrum, suggesting a pancreatic pseudocyst.

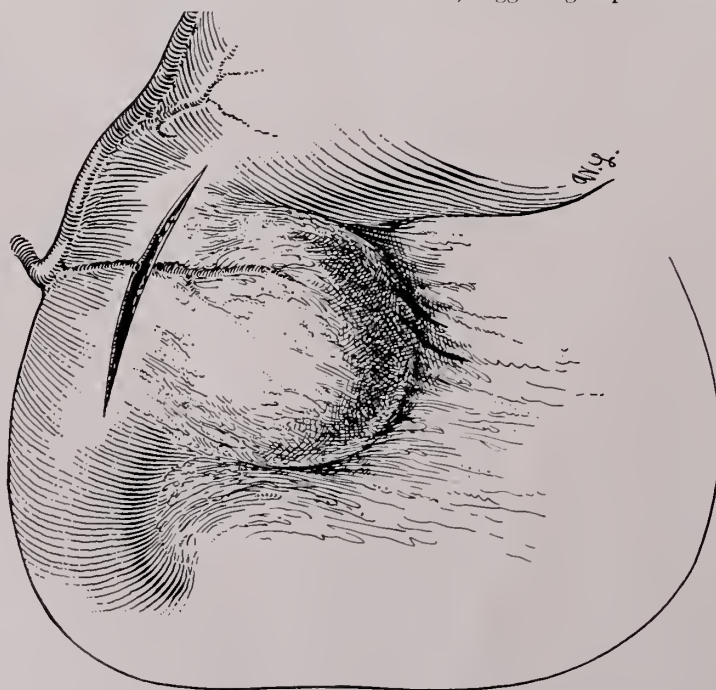


Fig. 2—Artist's impression of the appearance at operation.

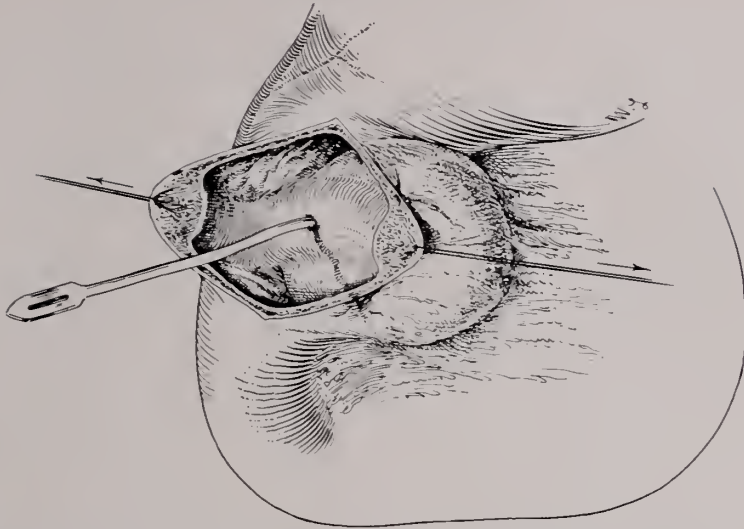


Fig. 3—This is the appearance after pylorotomy demonstrating communication into duplication.

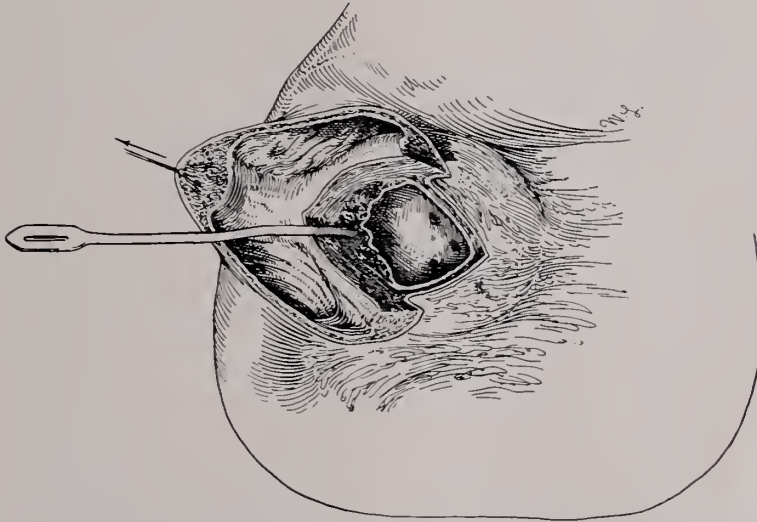


Fig. 4—Further dissection illustrating pancreatic communication and interstitial inflammation involving the common wall.

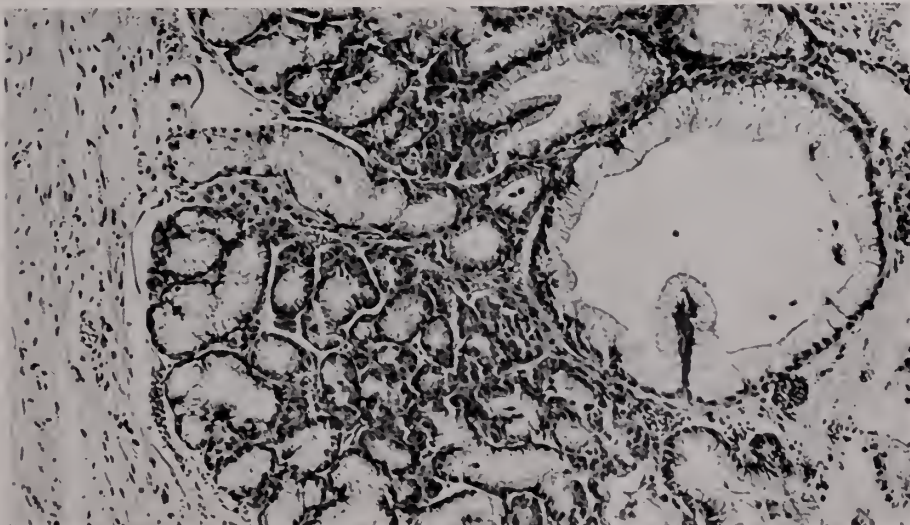


Fig. 5—Microscopic section of the gastric mucosa present in the duplication.

Ladd as hollow structures lined with epithelium similar to that found in the intestinal tract. The muscular coat, usually two-layered, is intimately adherent to and microscopically a part of the contiguous alimentary tract. This case satisfied these criteria. Gastroduodenal duplications are the rarest type.^{1,2} We consider our example to be more likely gastric since it was so lined and was contiguous, at least in part, with the stomach. However, a definite distinction cannot be made since these features are not exclusive. Thirteen per cent of duodenal duplications have gastric mucosa, and more of these communicate with the adjacent bowel or first appear in later life (33% over 20 years of age).³

Schuster and Castleman⁴ report a "muscular" cyst in a five-year-old boy which, although lined with gastric mucosa, communicated with the pancreatic duct. Their patient also had evidence of pancreatitis. Bradbeer⁵ reports a similar case in a 17-year-old white male without evidence of pancreatic inflammation. However, in both of these cases the cyst could be completely excised after ligation of the pancreatic ducts, since in one

it was only loosely attached to the stomach wall and in the other was lying free in the lesser sac.

Aberrant pancreatic tissue has been seen in the wall of gastric and duodenal diverticula; however, in none of these has direct communication with the normally situated pancreas been present. Aberrant pancreas has not been described in duplication cysts of the stomach. McLetchie⁶ reports an infant with a duplication arising from the first part of the duodenum surrounded by annular pancreas. The lesion extended superiorly and herniated through the diaphragm into the thorax posterior to the esophagus.

Obstruction to the stomach is common with duplication cysts. Bishop and Koop⁷ show a roentgenogram of a duplication comprising the antrum, pylorus, and proximal duodenum which has a strikingly similar appearance to our case. In the latter, extrinsic pressure was compounded by inflammation as a result of interstitial rupture of the cyst, presumably secondary to peptic ulceration. It is also possible that the opening of the duplication into the pylorus became ob-

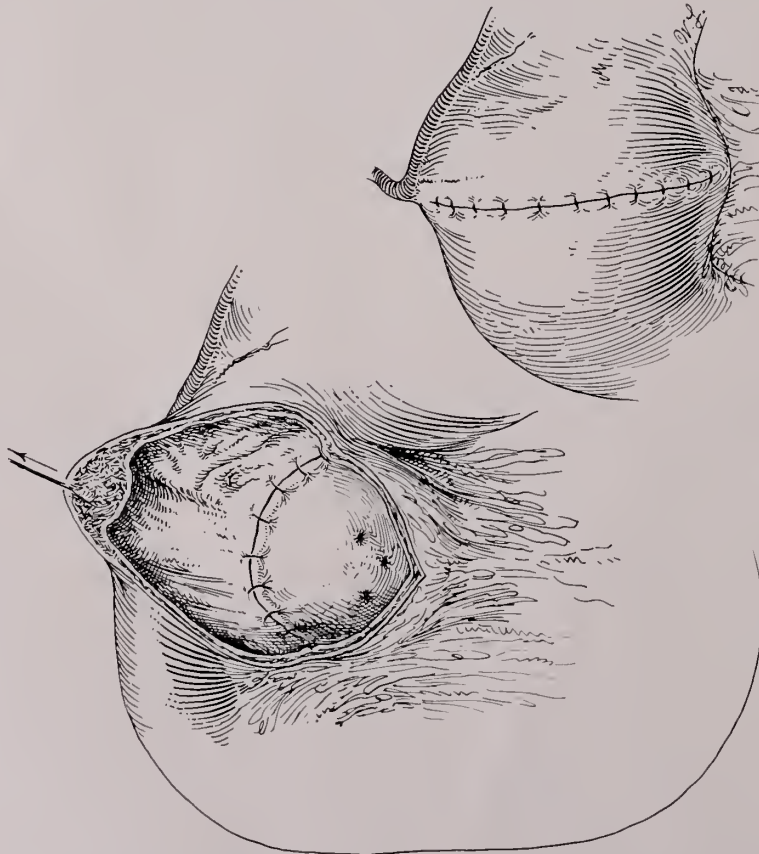


Fig. 6—Schematic illustration of the closure which included removal of the common wall and Heinecke-Mikulicz pyloroplasty.

structed intermittently, resulting in episodic hyperamylasemia similar to that described in vomiting or after duodenal distention. It was interesting that there was no evidence of previous pancreatic necrosis or pancreatitis at the time of surgery as was anticipated preoperatively. The opening into the stomach was probably not an acquired fistula but was congenital, as was the pancreatic drainage, since there was no fibrosis or other signs of inflammation of the stomach itself.

Treatment in our case consisted of internal drainage which is now the generally accepted method, resection being considered unnecessary.⁷ Histologic sections revealed the mucosa of the cyst to contain chief cells, thus resembling fundic mucosa. In Schuster's case an ulcer was found in the mucosa. There is some risk to incorporation of a gastric-lined cyst so close to the duodenum since, if the mucosa is predominantly antral, one could expect to have chronic release of gastrin from alkaline stimulation. However, our patient has remained asymptomatic for three years, making this complication unlikely. It is interesting that she has gained over 50 pounds in weight, although previously a thin woman, suggesting that she had been partially obstructed for some time.

In summary this case is important not only because it is apparently unique, but since it links the two previously described examples of a gastric-lined muscular cyst arising in the pancreas with the relatively common cases of aberrant pancreatic tissue within the wall of an otherwise normal stomach.



Fig. 7—Patient's appearance three years postoperatively.

References

1. Abrami, G. and Dennison, W. M.: Duplication of the stomach. *Surgery*, 49:794, 1961.
2. Owen, H. W., Holman, C. B. and Priestley, J. T.: Duplication of the Stomach: Report of a Case. *Proc Mayo Clin* 29:228, 1954.
3. Thompson, N. W. and Labow, S. D.: Duplication of the Duodenum in the Adult. *Arch Surg* 94:301, 1967.
4. Schuster, S. R. and Castleman, B.: Pancreatic and Abdominal Mass in A Five Year Old. *New Eng J Med*. 270:736, 1964.
5. Bradbeer, T. W.: Unusual Foregut Anomaly: An Extragastric Pouch Communicating with Pancreatic Duct. *Brit J Surg* 46:603, 1958-59.
6. McLetchie, N. G., Purves, J. D. and Saunders, R. L.: The Genesis of Gastric and Certain Intestinal Diverticula and Enterogenous Cysts. *Surg Gynec Obstet* 99:135, 1954.
7. Bishop, Harry C. and Koop, E.: Surgical Management of Duplication of the Alimentary Tract. *Amer J Surg* 107:434, 1964.

At a certain age some people's minds close up; they live on their intellectual fat.

William Lyon Phelps

Gargantua?

For centuries intemperance in eating was not frowned upon but taken for granted. An English country gentleman's dinner in 1768 included:

A roasted Shoulder of Mutton and a plum Pudding—Veal Cutlets, Frill'd Potatoes, cold Tongue, Ham and cold roast Beef, and eggs in their shells. Punch, Wine, Beer and Cyder for drinking.

And when the same Rev. James Woodforde gave an "elegant" dinner in 1774, it consisted of the following:

The first course was, part of a large Cod, a Chine of Mutton, some Soup, a Chicken Pye, Puddings and Roots, etc. Second course, Pidgeons and Asparagus. A Fillet of Veal with Mushrooms and high Sauce with it, roasted Sweetbreads, hot Lobster, Apricot Tart and in the Middle a Pyramid of Syllabubs* and Jellies. We had Dessert of Fruit after Dinner, and Madeira, White Port and red to drink as Wine.

A dinner served at the United States Hotel in Saratoga Springs in August, 1890, included:

	Oysters on Half Shell	
	Sauterne	
Green Turtle Soup		Olives
Boiled Salmon		Potato Balls
	Lobster Sauce	
	Sauterne	
Sweetbread Cutlets		Peas
	Claret	
Fillet of Beef		Mushroom Sauce
Lima Beans		Mashed Potatoes
	Champagne	
	Roman Punch	
Supreme of Chicken		Truffle Sauce
Terrapin		Saratoga Chips
Partridges on Toast		Salted Almonds
Lettuce		Crackers
	Cheese	
	Roquefort and Neufchatel	
	Meringues	
	Cigars	
Ices		Fruits
Coffee		Benedictine

*Editor's Note: Today such a dinner would not be considered a treat but a torture or would it?**

—Henry Sigerist, M.D.: Civilization and Disease.

* See Test Your Word Score Page 1227.

** See Foodie, Minnesota Med 46:663, 1963.

The whole prospect and outlook of mankind grew immeasurably larger, and the multiplication of ideas also proceeded at an incredible rate. This vast expansion was unhappily not accompanied by any noticeable advance in the stature of man either in his mental faculties or his moral character. His brain got no better; but it buzzed more.

—Winston Churchill, 1949

Cardiac and Pulmonary Dyspnea

Clinical Differentiation

DAVID E. DINES, M.D.*
THOMAS W. PARKIN, M.D.
Rochester, Minnesota

ALTHOUGH SHORTNESS of breath is a symptom of various diseases it generally can be classified as one of two types: cardiac or pulmonary dyspnea. The differentiation is important because the treatment is not the same in the two conditions, and the prognosis depends on the correct diagnosis and the proper treatment. The patient with chronic obstructive pulmonary disease and dyspnea can experience respiratory acidosis and coma and can die from being placed in an oxygen tent after receiving morphine sulfate. The patient with coronary insufficiency and pulmonary edema, however, might be improved with an oxygen-tent environment and parenterally administered morphine sulfate. The following two cases in which the presenting symptom was dyspnea illustrate some of the practical aspects in the differentiation of cardiac and pulmonary dyspnea.

Report of Cases

Case 1

A 66-year-old man was seen for the first time on Nov. 18, 1966, because of progressive shortness of breath of seven years' duration; he had been unable to work for the preceding six years. He had smoked one to two packs of cigarettes per day for 50 years and for 20 years had been bothered by a chronic cough which produced one to two ounces of sputum per day. Cold air, fumes, and dust caused him to become choked up and dyspneic.

On physical examination, dyspnea of grade 4 and expiratory slowing of grade 4 were noted. The antero-posterior diameter of the thorax was increased, the chest was tympanitic to percussion, and the diaphragm moved less than 1 cm. bilaterally.

Chronic obstructive pulmonary disease with emphysema and chronic bronchitis was diagnosed.

A chest roentgenogram (Figure 1) showed evidence of emphysema, with hyperaeration in the lower lung fields and fibrosis in the upper. An induced sputum was negative for fungi and acid-fast bacilli. The electrocardiogram showed a pattern of P pulmonale, left axis deviation of QRS, and marked respiratory variation with an S wave in V_1 and V_2 (Figure 2). The actual pH was 7.38 and the pCO_2 was 61 mm. Hg., indicative of a compensated respiratory acidosis (Astrup method). Tests of pulmonary function (Table) show a marked, chronic obstructive pattern.

*Mayo Clinic and Mayo Foundation: Section of Medicine.

A program of therapy for chronic obstructive pulmonary disease was instituted, consisting of the use of a bronchodilator (isoproterenol by nebulization with an air compressor), breathing exercises, and administration of fluids; and the patient was instructed to stop smoking.

Case 2

A 66-year-old white man was seen April 23, 1965, because of dyspnea, nocturnal wheezing, cough, and hemoptysis of seven days' duration. He had been examined on July 21, 1964, for angina and again on March 31, 1965, for angina and bronchitis. He had been a known diabetic for two years and had had an anterior myocardial infarction in July 1964.

Physical examination disclosed an early, short systolic ejection murmur at the left sternal border. The pulmonic valve closure sound was increased in intensity. Diffuse moist rales were heard posteriorly, and the liver edge was palpable 4 cm. below the right costal margin. There was no peripheral edema.

A chest roentgenogram (Figure 3) showed the "butterfly" pattern of acute venous pulmonary hypertension. An electrocardiogram (Figure 4) showed a pattern indicative of an old anterior myocardial infarction.

The patient was treated with diuretics and digitalis. He lost 13 lbs. in nine days and the dyspnea disappeared. A second chest roentgenogram, taken nine days after the first (Figure 5), showed that the heart size was normal.



Fig. 1 (Case 1). Chest roentgenogram showing hyperaeration, depressed diaphragms, and prominent main pulmonary arteries in chronic obstructive pulmonary disease with emphysema. There is fibrosis in both upper lung fields.

TABLE
Pulmonary Function

Function	Estimated normal	Before treatment
Pulmonary volumes		
Expiratory vital capacity, L	4.6	1.69 (2.00)*
Inspiratory vital capacity, L		
Residual volume, L	1.5	5.09
Total capacity, L	6.1	6.78
RV/TC $\times$ 100, %	≤ 45	75
Functional residual capacity, L	2.7	5.81
Expiratory reserve, L	1.2	0.72
Maximal breathing capacity, L/min.	85	17 (19)*
Maximal midexpiratory flow, L/sec.	≥ 2.0	0.3 (0.3)*
Expiratory slowing, grade	0	4 (4)*
Nitrogen washout index, N ₂	≤ 2.5	2.7
Arterial oxygen saturation (oximeter), %		
Resting (air)	95-98	95
Resting (oxygen)	100	100
Before exercise (air)	95-98	98
Exercise (air): 1.0 min.	No fall	99
After exercise: 0.5 min.		98
Exercise (oxygen)	100	
Ventilation (sitting rest, breathing oxygen)		
L/min.		10.98
Rate, respirations/min.		27.6
Average tidal volume, ml.		398
CO diffusing capacity		
Rest: Test, 7 ml/min/mm. Hg. Normal, 17		

*Values after treatment in parentheses.

Discussion

Dyspnea on the basis of primary lung disease can result from an inability to ventilate, a restriction of the lung volumes, an impairment of diffusion of gas across the alveolar-capillary membrane, and a decreased efficiency of the chest bellows. Each type will increase the work of breathing.

Dyspnea in the cardiac patient results from secondary changes in the lungs. There is a rise in left atrial pressure due to obstruction of the mitral valve (mitral stenosis) or to incomplete emptying of the left ventricle in left ventricular failure. The rise in left atrial pressure is followed by pulmonary vascular engorgement and an increase in pulmonary capillary pressure. The increase in pulmonary capillary pressure causes a transudation of fluid into the interstitial tissue and results in the lungs becoming less compliant. This loss of compliancy increases the work of breathing.

Differential Diagnosis

In the differential diagnosis of cardiac and pulmonary dyspnea, the history and physical examination are most important. *Dyspnea from chronic obstructive pulmonary disease* has an insidious onset, as shown in Case 1 (seven years). The patient usually has a 20- to 50-year history of cigarette smoking, a long history of chronic cough, and a history of wheezing and cough when exposed to dust, fumes, high humidity, and cold air. *Dyspnea of left ventricular failure* is more abrupt in onset, as illustrated in Case 2 (seven days). At first the dyspnea may be evident only with exertion, but without treatment there will be progression to dyspnea at rest, orthopnea, and paroxysmal nocturnal dyspnea. Cough was of long duration and was productive of sputum in our first case, whereas it was paroxysmal, nocturnal, and of short duration in our second case.

Physical examination will often reveal that the dyspnea is of pulmonary origin. There usually will be an increase in the anteroposterior diameter of the thorax, hyperinflation of the lungs, decreased motion of the diaphragms, and expiratory slowing. All of these findings were present in Case 1. If *pulmonary fibrosis* is present, there are characteristic leathery, crackling rales at both

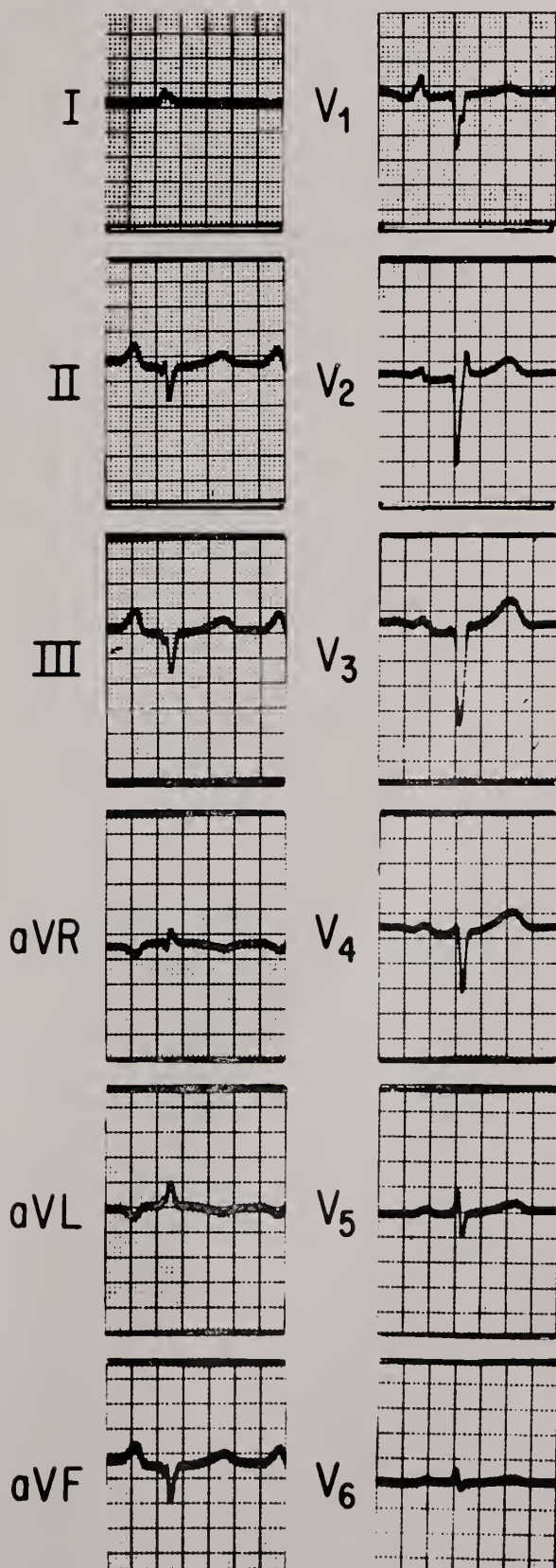


Fig. 2 (Case 1). Electrocardiogram showing P-pulmonale pattern and S waves in V₁ and V₂.

bases, hyperventilation, and restricted breathing. In the cardiac patient there usually are crepitant rales heard posteriorly in the lung bases; coughing will not clear the rales, as it so often does in chronic bronchitis. A diastolic ventricular gallop sound, atrial fibrillation, and cardiac enlargement may be evident. It should be mentioned that patients with chronic obstructive pulmonary disease can present with right ventricular failure, hepatomegaly, and peripheral edema, but the basic points in history and physical examination of the lungs mentioned previously will still be evident.

X-ray Findings

The chest roentgenogram may be helpful in the differential diagnosis. Roentgenographic study may show *no abnormality in chronic obstructive pulmonary disease* or may reveal hyperinflation, widened interspaces, an increased anteroposterior diameter, and flattened diaphragms (Figure 1). The heart size may be normal, but in *cor pulmonale* it is important to look for prominent main pulmonary arteries. This finding was most helpful in our study of 52 patients with *cor pulmonale*, in which 48% showed prominent main pulmonary arteries on the routine roentgenogram of the thorax.¹ If there is pulmonary fibrosis the



Fig. 3. (Case 2). Chest roentgenogram (April 23, 1965) showing butterfly pattern of acute venous pulmonary hypertension with cardiomegaly.

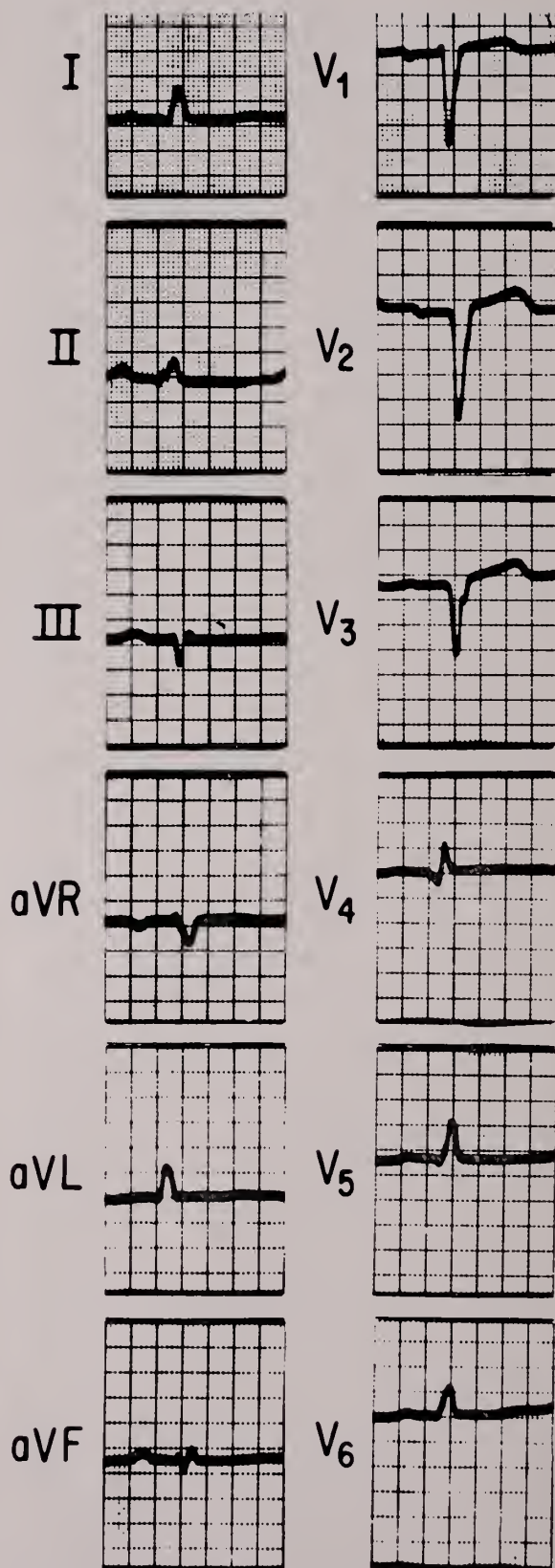


Fig. 4 (Case 2). Electrocardiogram showing pattern of an old anterior infarction.

chest roentgenogram will demonstrate a diffuse symmetric infiltration, but the heart size will remain normal. In *left ventricular failure*, a comparative film may show a recent increase in heart size and an increase in the pulmonary vascular markings or "butterfly-like" densities radiating from the hilar areas, as is shown in our second case (Figure 3). The roentgenogram of the chest in congestive failure also may be of help if Kerley lines (interlobular septal lines),² interlobar collections of fluid, and bilateral pleural effusions (predominantly right pleural) are present.

Pulmonary Function

Tests of pulmonary function can be of help in determining whether the dyspnea is of pulmonary origin. Pulmonary function (Table) in our first case shows a typical pattern of diffuse obstruction to airflow. In left ventricular failure, there can be a decrease in vital capacity and loss of compliance, but the maximal breathing capacity is preserved and there is no air trapping.

The electrocardiogram can be helpful, as it was in our two cases. Case 1 had the typical P-pulmonale pattern³ with tall peaked P waves in II and V₁ and deep S waves in V₁ and V₂ (Figure 2). The presence of a P-pulmonale pattern with right ventricular hypertrophy would lend support to a possible diagnosis of chronic obstructive pulmonary disease. A broad notched P wave in II, III, and a VF and a typical PV₁ pattern⁴ would lend support to left atrial enlargement if mitral valve disease was the cause of the pulmonary congestion. Especially important is the finding of an old or a recent myocardial infarct, as was demonstrated in our second case (Figure 4). This finding lends support to the explanation that the dyspnea was caused by left ventricular failure from coronary insufficiency and previous anterior myocardial infarction.

Treatment

Treatment is important but should not be used as a therapeutic test. The diagnosis should be made prior to beginning treatment. Therapy with digitalis and diuretics is indicated in dyspnea due to cardiac disease, and bronchodilat-



Fig. 5. (Case 2). Chest roentgenogram (May 1, 1965) after digitalization and diuretics.

ing drugs (isoproterenol) are used to improve ventilation in chronic obstructive pulmonary disease. However, we have seen patients who are receiving digitalis and diuretics who have been found to have primary pulmonary disease, and who need bronchodilating medication to improve their ventilation.

Dyspnea on a functional basis⁵ must always be considered in the differential diagnosis. In some instances, functional dyspnea can be suspected, but only by means of a complete history, physical examination, pulmonary function tests, roentgenogram of the chest, and electrocardiogram can such dyspnea be proved to the patient.

Summary

In the clinical differentiation of cardiac and pulmonary dyspnea, an accurate diagnosis as to the cause of the dyspnea is important for proper therapy and improved prognosis. In many cases, an accurate differentiation can be made only after a careful history is taken, a physical examination is conducted, and pulmonary function studies, roentgenograms of the chest, and electrocardiograms are made.

References may be secured from the author or the reprints.

Sometimes a go-getter is sorry he gotter.—Herbert Prochnow

WHAT'S YOUR DIAGNOSIS?

This 61-year-old man was found unconscious at the wheel of his parked car by the police. He had left home less than one hour earlier, feeling well. He had a long history of congestive heart failure, asthma, eczema, emphysema, cortisone use, and osteoporosis with multiple vertebral compression fractures. He had been unable to work for two years, but at the time of this final catastrophe he was up and about and "feeling better than he had in years."

In the emergency room he was cyanotic, pulseless, blood-pressureless, and unconscious. Administration of intravenous fluid, cortisone, and aramine was started. An EKG showed atrial fibrillation and cor pulmonale; a chest x-ray was normal except for the emphysema. Blood sugar was 385 mg% (but the intravenous had already been started). The wbc. was 20,600, the Hgb. 13 Gm. CO₂ 16, K 5.3 Cl 95, Na 135. After about an hour in the emergency room, he regained consciousness enough to name his doctor and to say that he was short of breath but had no pain.

Two hours after admission he was still alert and coherent, but unable to remember anything that had happened or how he got to the hospital. His extremities were cold, cyanotic and pulseless; his pupils were fixed and dilated, and his blood pressure could not be detected.

Four hours after admission he was seen by a medical consultant who felt that he was less responsive than earlier, but noted no other changes in his condition. He agreed that some sort of cardiovascular collapse had occurred and ordered chloromycetin for the white count, bicarbonate for the acidosis, pronestyl for the arrhythmia, levophed for the blood pressure, and an increase in the solu-cortef to 500 mg. every two hours.

Eight hours after admission a distended, tympanitic abdomen was first noted; but the patient was again comatose and still pulseless with no blood pressure. Twelve hours after admission he was dead.

What's Your Diagnosis? Turn to page 1189.

The Corset*

The corset is a product of the baroque period.** Baroque art broke the noble straight line of the Greek pillar and replaced it with the spiral column, developing an architecture of spirals and curves and bulges.

The corset was probably responsible for many of the vapors, faints and fits that befell 18th century ladies. The tighter it was worn, the worse were its effects on health. By compressing the lower part of the chest and the abdominal muscles, it seriously impaired respiration. The corset also deformed the liver, compressing it and displacing it as well as the stomach and other abdominal organs; it exerted pressure on the blood vessels so that respiration, digestion and circulation were badly affected. There is hardly a disease that has not been attributed to the corset. If anything, the corset made the fair sex a weak sex.

—Henry Sigerist, M.D.: *Civilization and Disease*

* See Page 1189.

** Baroque Period—the period from the 16th to the 19th century when art and architecture were characterized by dynamic and extravagant curves and scrolls.

Drugs and Doctors*

Problem in the Production of Certain Behavioral Disorders

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AS WE REVIEW the history of any drug, we commonly find a great burst of enthusiasm for its use when it is first introduced to medicine. Fortunately this enthusiasm is often justified by the clinical response of the patient. With this enthusiasm, however, some of the complications or untoward side-reactions to the drug are overlooked or missed completely. This is especially significant in view of the recent and current prolific production of new therapeutic agents. Even with well-recognized and long-established drug programs it is not unknown for subtle side-reactions to go unrecognized for long periods. Not all behavioral disorders are neurotic or psychotic in origin. They may be induced by drug therapy, especially in marginally adjusted persons, who seem to have a greater tendency toward adverse reactions to drugs.

The cooperative evaluation of the patient by the internist and the psychiatrist will usually lead to proper recognition of the disorder. We emphasize this mutual concern for the patient. It is almost always necessary for accurate classification and management of the problem.

It is also important to recognize the part that the illicit, inappropriate, or excessive use of drugs may play in the reaction or disorder that we may see in a patient. People learn to use drugs. They learn this most broadly from the culture itself. Generally, a wide variety of drug experience is associated with childhood illness and exposure to physicians, use of medications at home during the formative years, enjoyment of illness because of the pleasant attention it elicits, childhood and adult eating problems for which various drugs are taken with or without medical counsel, and, in adults, cravings for foods and drinks, visits to the physician, and the ultimate and consequent prescribing of more medication.

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†Section of Psychiatry, Mayo Clinic and Mayo Foundation.

We are indeed a culture which uses drugs extensively. The enormity of the problem is suggested by the fact that in 1963 drugstores in the United States filled more than 60 million prescriptions for tranquilizers and more than 45 million for barbiturates. These drugs are used in medical care, in home remedies, for keeping awake and going to sleep, and of course socially, as in the use of alcohol. More privately, people may use alcohol, take an antidepressant drug, a tranquilizer, or a barbiturate, smoke marihuana, or sniff glue or gasoline.

Of more significance to our thesis, however, is the part we as physicians play in the genesis of these drug-induced disorders. In conjunction with the prolific production and use of all types of drugs, behavioral reactions are being encountered more frequently. Because the onset of these symptoms may be insidious and subtle or may precisely mimic an organically induced disorder, the role played by drugs is often overlooked. The problem is common to all fields of medicine. Most classes of drugs may be involved at times in contributing to a behavioral reaction. The compounding of medication by the patient himself or even by the physician who, when he prescribes a new drug, fails to admonish the patient to stop taking a previously-prescribed drug, makes the problem more involved. With more and more patients seeking specialized care for each of their problems (for example, seeing a gynecologist, a cardiologist, a urologist, and a general internist concomitantly for separate problems), the patient frequently ends up with similar medicaments from several physicians, each of whom was unaware of what his colleague had prescribed. It is obvious that this excessive medication often becomes a complex problem for the physician as well as for the patient.

We will present four cases as illustrations to point out the urgency for recognition of the part played by drugs in the development of a behavioral disturbance. They illustrate the need for constant vigilance to avoid these adverse reactions.

Reports of Illustrative Cases

Case 1. Impulsive Rage Reaction.

A 23-year-old college senior was brought to the hospital emergency room by her parents because of personality change, unsteadiness of gait, slurring of speech, diz-

ziness, and cloudiness of vision of three weeks' duration. Four days prior to admission she had driven her car off the road, claiming afterward that she had suddenly lost her vision. During the intervening three or four days the patient became increasingly talkative and argumentative and began swearing at her parents. She attempted to contact the local sheriff and a local attorney to enlist their aid in her leaving home, and her parents found it necessary to restrain her forcibly from leaving the house at night.

She was a 5-foot, 1-inch overweight, very heavily mascaraed, peroxide blond who chattered constantly, loudly, and argumentatively during the entire examination. Her speech was heavily slurred and her gait was markedly ataxic. Her pupils were widely dilated and there was gross horizontal and vertical nystagmus.

It was ascertained that she had started taking a methamphetamine-phenobarbital preparation to control her appetite during a weight reduction program five years before, and she had continued taking the tablets in larger amounts (five to six tablets daily) because she found that they stimulated her to such a degree that she could do more schoolwork.

With cessation of all medications her symptoms progressively abated and she became symptom-free. The diagnosis was an impulsive rage reaction secondary to use of a methamphetamine-phenobarbital preparation. She was referred to a local psychiatrist for follow-up psychotherapy.

Case 2. Acute Hallucinosiis.

A 48-year-old housewife complained of generalized fatigue and aching, mostly in the hips and legs, of eight years' duration. She had been taking meprobamate, one tablet (400 mg.) four times a day, for eight years, and in the month prior to coming to us she had increased this to eight or ten times a day. She then abruptly stopped the medication, following which she complained of insomnia and anxiety and suffered anxiety attacks with hyperventilation. Subsequently, she developed hallucinations, delusions, and agitation, requiring admission to the closed psychiatric ward.

The results of physical examination and laboratory tests were normal. A Minnesota Multiphasic Personality Inventory (MMPI) gave results consistent with a psychoneurotic depression.

The history revealed that the patient had a great deal of difficulty with her mother. In addition, she was fearful of becoming pregnant.

When this patient was admitted to the closed ward she was actively hallucinating and was delusional with paranoid ideation, but she was not disoriented. She was given 200 mg. of chlorpromazine (Thorazine) per day; within a three-day period her psychosis subsided and the chlorpromazine was discontinued. After this episode she had no further somatic complaints. She was not interested in any uncovering psychotherapy. She was dismissed without any drugs. The diagnoses were: "psychoneurosis with somatization; acute hallucinosiis secondary to meprobamate withdrawal."

Case 3. Paranoid Confusion.

The third patient was a 59-year-old man who had been in excellent general health but, because of "feel-

ing a little under the weather," went to his local physician, who found no abnormalities. A thoracic roentgenogram showed what appeared to be a huge cardiac silhouette. Although he had no cardiac symptoms, the patient was started on digitoxin. It was later estimated that he was taking 0.6 mg. of digitoxin daily. Eight or nine days later his family brought him to the hospital, stating that he had voided on the living-room rug, that his speech was "bizarre and disconnected," and that he acted very suspicious toward everyone.

On admission to the hospital it was noted that his heart rate was 36 beats per minute, and an electrocardiogram disclosed complete AV block. The thoracic roentgenogram showed a cardiac silhouette which was normal but almost entirely obscured by a large anterior mediastinal shadow that proved to be a large lipoma.

The digitoxin therapy was discontinued and after a week his heart rate and his cerebration returned to normal.

The diagnosis was "paranoid confusion secondary to digitalis toxicity."

He was advised that digitalis was not indicated in his case, and, when seen six months later, he continued to feel and act well.

Case 4. *Delusions of Grandiosity.**

In this example the patient was a 51-year-old white man who had been troubled with rheumatoid arthritis for 10 years. He said he was unable to take aspirin because it upset his delicate stomach. He had tried enteric-coated aspirin but complained that it also upset his stomach. He had been known to believe that two to three times the prescribed dose of a medicine would give two to three times the beneficial effect, ignoring the possible toxic or harmful results of such dosage. Until the previous few years he had been whimsical and jovial and had enjoyed writing clever humorous rhymes. He had always worked very hard and had very few interests outside of work. He always wanted things done immediately, was impatient, would not delay, and was bossy and demanding of his help or partners. He began giving himself cortisone injections 15 months before he was seen by us. Ten days before his consultation he told his son-in-law, who manages his farm, that he had

given himself 40 times his usual dosage of cortisone that day. He had apparently followed a very irregular schedule of cortisone dosage for the previous year. He had suffered a financial setback three months before hospitalization "when he guessed wrong in the grain market." He had been noted to have a flushed, red, and swollen face for three months. For two months he had complained of dizziness on standing. For the most recent month he had begun to get ideas of grandiosity. "The farm began looking like Grand Central Station" in the words of his son-in-law, because he had hired so many people to build new buildings and fix fences, and he had bought many hogs to feed. He always had been pleasant to his wife until eight days before hospitalization, at which time he became verbally abusive to her. He also began writing checks for large amounts of money to strangers.

Hospitalization and reduction of his corticosteroid dosage over a period of two weeks resulted in symptomatic remission. The diagnosis was "delusions of grandiosity secondary to hypercortisonism."

Summary

Overprescription and overmedication often lead to drug toxicity. Four clinical examples are given to stress the diverse behavioral reactions that can result from inappropriate use of common drugs. Indolence in drug prescribing may present problems for the patient; catering to a patient's demands for immediate relief invites disaster. The physician has great need to review the criteria of indications for drug therapy and to continue to base such therapy on the solid tenets of a physical examination and an astute evaluation of the patient's psychosocial environment. Then he can expect that the proper drug will be used in the proper dosage with a satisfactory result.

* See Test Your Word Score Page 1227.

ANSWER TO WHAT'S YOUR DIAGNOSIS

(From page 1186)

At autopsy there was found a dissecting abdominal aneurysm with hemorrhage into both adrenals and kidneys. This case is proof that cortisone cannot cure everything, and that absence of pain does not indicate absence of organic pathology. The case was instructive because of the complete lack of abdominal physical findings until the case was terminal.

Etymologically Speaking

**Corset*—a stiff, tight undergarment for women, designed to exaggerate body curves—from French *corps* (body).

* See Page 1186.

First Use of Ether Anesthesia

In the National Statuary Hall in Washington, D. C., Dr. Crawford W. Long's statue bears the inscription: "Discoverer of the use of sulphuric ether as an anesthetic in surgery, on March 30, 1842, at Jefferson, Jackson County, Georgia."

Long had come to Jefferson to set up his practice in 1841, shortly after his graduation from medical school in Philadelphia. Soon hereafter, a "laughing gas" showman intrigued the townspeople of Jefferson with a lecture on the strange effects of nitrous oxide. Anxious to try the gas for themselves, several people asked Dr. Long for a sample. As it happened, the young doctor did not have any on hand but he did have some ether, which, he assured them, would have about the same effect.

Some young men tried the ether in Long's office, became exhilarated, staggered about, laughed and behaved more or less as expected under the circumstances. But Long, more observant than most, noticed that as they staggered and stumbled about, bumping into furniture and bruising themselves, they seemed to feel no pain. Nor did he, himself, have any recollection of pain after joining the ether party and later finding bruises on his body. This set him to wondering about the possibilities of ether. If a small amount of it could mask the pain of a bruise, would a larger amount be able to prevent the more extreme pain of surgery?

Dr. Long answered this question on March 30, 1842. James M. Venable, a participant in the ether experiments, had some tumors on his neck which he had delayed having removed because of his fear of pain. Long suggested that the use of ether might permit a painless operation. Venable agreed to its use. That night Dr. Long poured some ether on a towel and held it over the patient's nostrils until he fell asleep. When Venable awoke, he was astounded to learn that one of his tumors was gone. He had felt absolutely no pain during its removal. The first operation under ether anesthesia was a success and the fee, incidentally, was two dollars.*

* Bernard Seeman: *Man Against Pain*

A Powder Is A Powder!

Ignorance continued sometimes to amuse, more often to anger, doctors. Dr. Ferdinand Herff, who practiced among Texas homesteaders, prescribed seven powders for a farmer's wife who was experiencing severe constipation. The price of the powders seemed high to the farmer, so he went home, and under the supposition that a powder is a powder, gave his wife seven doses of gunpowder instead. When the doctor stopped by to see how the woman was getting along, he found her no better and decided he must give her an enema. He told the farmer, "Bring me two chairs, a syringe, hot water and a lamp.

"Doctor, I bring you the chairs, the syringe and the hot water," said the farmer, turning pale, "but I don't bring you the lamp. That woman has seven charges of gunpowder in her."*

*Richard Dunlop, M.D.: *Doctors of the American Frontier*

Sweat Chloride Assay for Cystic Fibrosis

Using
Pilocarpine Iontophoresis
Stimulation,
Filter Paper
Collection and
Cotlove Chloridometer
Analysis

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WHEN PROPERLY DONE, the assay of the chloride content in sweat is the most reliable diagnostic test for cystic fibrosis. It is also one of the most specific diagnostic tests in medicine when properly done, for true-false positive and false negative tests are almost unknown. Nevertheless, false positive and false negative tests are frequently seen when the test is not done correctly.

In this paper we describe the technique and safeguards we have developed over the past five years plus a simple method for evaluating the results. We use the pilocarpine iontophoresis method devised by Gibson and Cooke¹ with modifications. This test has three distinct steps: (1) stimulation of sweating, (2) collection of the sweat sample, and (3) analysis of the collected sweat.

Stimulation of Sweating

Equipment

1. Direct current power supply with high internal impedance to limit output, capable of delivering at least 1.5 amps, and preferably not more than 2.0 amps, direct current. ABC Oxygen Rental, 2722 East Lake Street, Minneapolis, Minn.
2. Wire leads—2
3. Two flat electrocardiogram type electrodes with a contact surface of about 5 sq. cm.
4. One perforated rubber strap—15" x 1"

Expendable Materials

1. Pilocarpine nitrate—10 gram lots, Mann Research Laboratories, 136 Liberty Street, New York, N. Y. 10006
2. Distilled water
3. Sodium nitrate — Mallinckrodt analytical grade
4. Gauze squares—4" x 4"
5. Rubber bands

*Department of Pediatrics, University of Minnesota Medical School.

This research was supported by grants-in-aid from the Minnesota Cystic Fibrosis Chapter and the National Cystic Fibrosis Research Foundation.

Reagents

1. Pilocarpine nitrate — 1.0% weight volume solution: 1 Gm. pilocarpine in 100 ml. distilled water, made fresh every two weeks and refrigerated between uses.
2. Sodium nitrate—2.0% weight volume solution: 2 Gm. in 100 ml. of distilled water.

Procedure

The electrodes are covered with a double layer of gauze to provide sufficient liquid-holding capacity to insure an even distribution of current and to prevent local hot spots. The gauze is secured to the electrodes with a rubber band. The loose ends of the gauze are trimmed to prevent direct contact between electrodes. (Fresh gauze is used on each patient.)

The electrodes are identified as negative or positive by their attachment to the iontophoresis transformer; the negative lead to the black outlet, the positive lead to the red outlet. The gauze covering the negative electrode is soaked with the 2% sodium nitrate solution. The gauze covering the positive electrode is soaked with the 1% pilocarpine nitrate solution. The soaked electrodes are then placed on opposite sides of the forearm with the positive electrode on the volar

surface (Figure 1). The rubber strap is fastened securely to assure good electrical transmission but not so tight as to cause pain or obstruct blood flow. The electrodes are held as flat as possible to insure an even distribution of current.

The iontophoresis transformer is turned on and the current gradually increased from 0 to 1.5 milliamperes over five to 10 seconds. The iontophoresis current is monitored constantly because slight burns may occur if the current is allowed to increase above 1.5 m.a. After five minutes, the transformer is turned off and the electrodes removed. Two, preferably three, tests are done on each patient, each test on a separate location on one or the other of the patient's arms.

Collection of Sweat Sample

Equipment

1. One forceps—bottle specimen, straight, blunt tip, nickel-plated steel
2. Desiccator, glass
3. Stoppered glass vials, diameter 2 cm., height 4 cm. with ground glass fittings

Expendable Supplies

1. Parafilm squares 2" x 2"

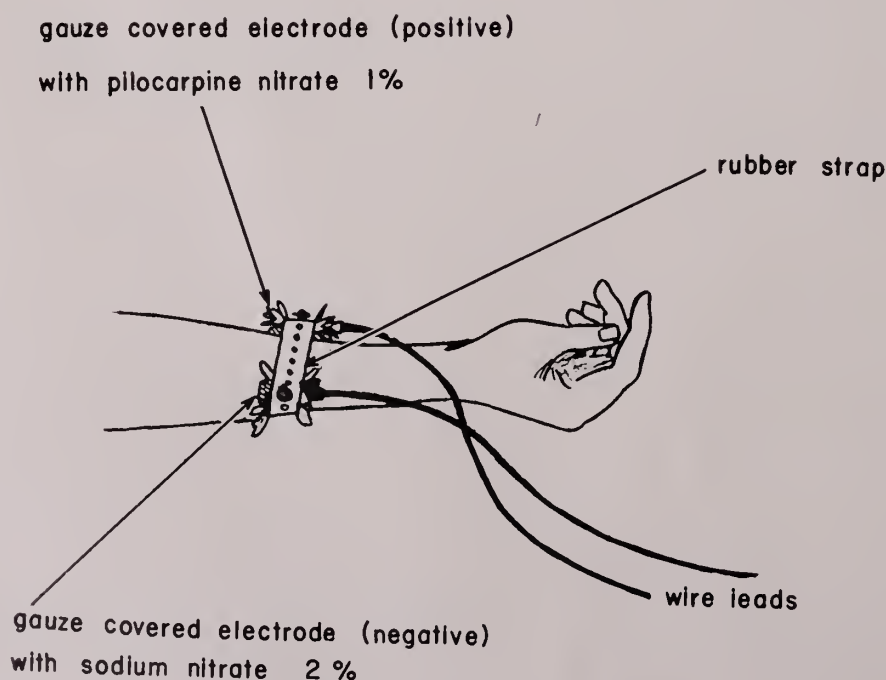


Fig. 1. — Position of electrodes for iontophoresis.

2. One inch adhesive tape—non-porous, water repellent
3. Filter paper 1 $\frac{1}{4}$ " diameter, chloride free, No. 470 Schleicher and Schuell Co., Keene, N. H.
4. Calcium sulfate, W. A. Hammond Drierite Co., Xenia, Ohio
5. Distilled water
6. Gauze squares

Precollection Preparation

The chloride-free filter paper and glass vials are dried over calcium sulfate before use. Glass vials and filter paper are handled with forceps or gauze and never come in contact with the technician's skin.

Collection Technique

After 24 hours of drying, one piece of the filter paper is placed in each glass vial. The stoppered vials and filter paper can be stored indefinitely in a desiccator in this manner. They are weighed to four-place accuracy on the day they are to be used and are placed in small paper bags on which the weight and identification number of the vial are recorded. After weighing, the vials are replaced in the desiccator until just before they are to be used.

The skin area under the positive electrode is washed with distilled water and dried with gauze. Forceps are used to remove the weighed circular piece of filter paper from the weighing bottle and to place it over the skin area where the positive (pilocarpine) electrode has been. The filter paper is covered with a parafilm square. The edges of the parafilm are taped firmly to the arm. An additional piece of tape is placed over any exposed parafilm to prevent the child from scratching or tearing a hole in it. The time is marked on both the tape and the paper bag. The empty weighing bottle is replaced in its paper bag and returned to the desiccator.

After 30 minutes one edge of the parafilm cover is lifted so that the moist piece of filter paper can be grasped with the forceps and quickly placed in the weighing vial from which it came. It is important that the moist filter paper be placed against the side of the weighing bottle to prevent shredding in the assay method to be described. The vial is stoppered and placed in its paper bag in the desiccator. A second weighing of the bottle is made. The weight of the

sample is the difference between the first and second weights. A minimum of 50 mg. of sweat is necessary for an accurate chloride determination.

Discussion

Mistakes made during the collection of the sweat sample can cause the analysis to give abnormally high or low values. The most obvious mistake is to permit evaporation and concentration of the sweat before the second weighing is made. Evaporation is most likely to occur during collection due to a poor seal on the parafilm which covers the filter paper, to delayed transfer of the sweat-saturated filter paper from the arm to the weighing bottle, or to a poor seal on the weighing bottle. If the filter paper disc comes in contact with the skin of the technician at any time, sodium chloride on his skin will cause contamination. Each of these errors will give falsely high sweat chloride values.

If the clean weighing bottle is touched by the technician's fingers, residual oils and electrolytes will adhere to the glass and be weighed as sweat. This error will cause a low sweat chloride value.

Assay of Chloride

Equipment

1. Chloride titrater—Aminco-Cotlove, American Instrument Co., Inc., 8030 Georgia Avenue, Silver Springs, Md. 20910.
2. Schuco autopipettes, 4 ml. chamber, Schuco Scientific Division of Schueller & Co., 250 West 18th Street, New York, N. Y. 10011.
3. Sample vials—40 mm. (height) x 18 mm. (inside diameter) with ground glass covers.
4. Kirk-type pipette or a calibrated micro constriction pipette with a 1% tolerance.
5. Glass rod
6. Forceps, straight without teeth
7. Glass vials, 5 cc. with plastic caps

Disposable Supplies

1. Distilled water
2. Sodium chloride—analytical reagent, Mallinckrodt
3. Acetic acid—analytical reagent, Baker
4. Nitric acid—reagent grade, Baker and Adamson
5. Gelatin reagent—American Instrument Co.

6. Acetone
7. Chloride free cleaning compound (Bon Ami)

Reagents

1. Chloride standard, 10 mEq/L. 584.5 mg. sodium chloride are dissolved in distilled water to make 1 liter of solution.
2. Diluent—to 900 ml. of distilled H₂O add 6.4 ml. of concentrated nitric acid and 100 ml. of glacial acetic acid.
3. Gelatin reagent—to 6.2 Gm. of dry mixture add approximately 1 liter of hot distilled water, swirl until clear. Dispense in 2-dram vials in amounts sufficient for one day's assay. The dispensed gelatin should be stored in a refrigerator and removed as needed. Unused portions of each day's gelatin should be discarded.

Pre-Analysis Procedures

Four ml. of diluent, automatically pipetted if possible, reduce the variability inherent in the technician's pipetting and 4 drops of 12% dextran with 4% glucose are added to the unknown sweat sample. The filter paper is flattened against the side of the vial with a glass rod.

Blanks are prepared by placing a disc of unused filter paper in a vial and adding 4 ml. of diluent. A clean forceps should be used in doing so to prevent chloride contamination. The filter paper is also flattened against the side of the vial.

Titration standards containing 1 micro equivalent (100 μ l. aliquot of 10 mEq/L standard sodium chloride) are prepared. The 100 μ l. aliquot is measured with a Kirk-type pipette or a calibrated micro constriction pipette with a 1% tolerance. The pipette used in preparing the titration standard is rinsed by sucking diluent up into the pipette twice. Distilled water, followed by acetone, is used to clean the pipette between duplicate pipettings.

Titration Techniques

The silver wire generator electrode which projects from the plastic rod at the right front is pushed down until its lower end is almost flush with the upper edge of the stirrer (Figure 2). This electrode is polished each day with the chloride-free cleaning compound. All titrations are done with the chloridometer set for low speed titration. After each titration, the chloridometer time should be set back to zero. Blank

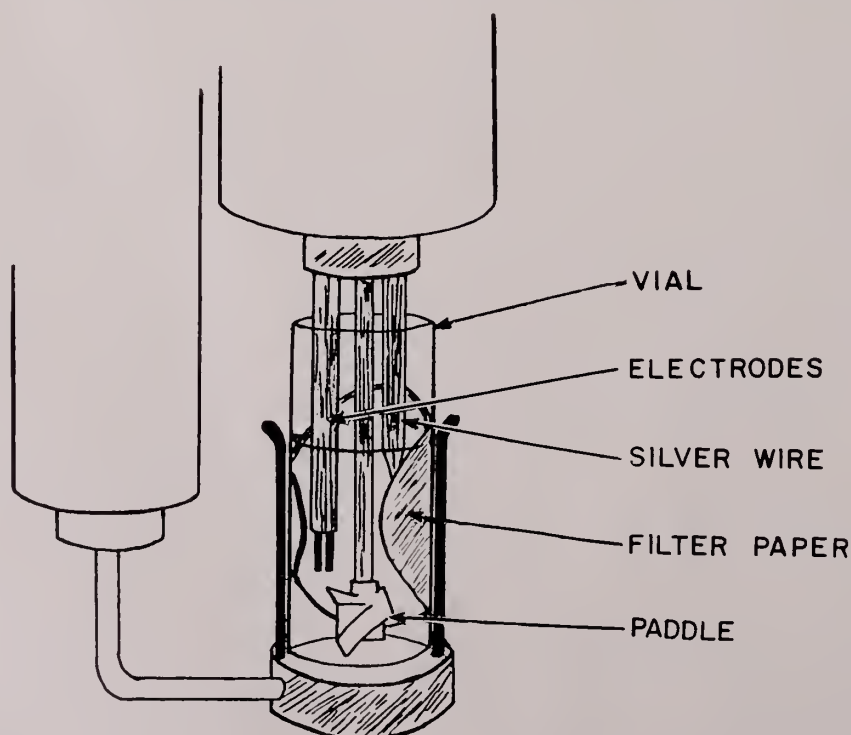


Fig. 2 — Illustration of vial containing filter paper with relationship to positions of the paddle, electrodes, and silver wire of the Aminco-Cotlove chloride titrator.

titration times must agree within one second. Three or four blanks may be needed before agreement is obtained. More than one second difference between repeated blanks may be due to insufficient chloridometer warm-up, inconsistency of filter paper, dirty electrodes, or contaminated glassware. The standards containing 1 mEq. of chloride, titrated in the same manner, must also not have titration time differences greater than one second. The unknowns are then run in the same manner, and their titration times recorded.

Discussion

If rubber is used in dispensing reagents, the sulfhydryl group released from the rubber will titrate as chloride and cause variable and falsely high values for sweat chlorides. Substitute plastic tubing for rubber tubing.

Oxidation of the silver electrodes also gives false high titration times. Titrate electrodes should be polished each day. Titrations run at medium or fast speeds will give less accurate results, particularly in small samples of low chloride concentration. Since the built-in error of the machine increases in significance as the titration time decreases, decrease the significance of the chloridometer's inherent error by using the low speed titration and increasing the titration time.

The end point of titration with the Cotlove chloridometer corresponds with the abrupt increase in current flow between the silver indicator electrodes produced when all the chloride in solution has been titrated and silver ions are still being released.² A false low reading will result if a short circuit is created by foreign material such as shredded filter paper or pieces of lint or gauze lodging between the indicator electrodes. Falsely high readings will occur if the paddle is stopped due to mechanical failure of the machine or blockage by the filter paper. The high reading is the result of the inability of the silver ions to circulate and combine with the chloride ions. The chloridometer technique gives results which are several times more consistent and precise than can be obtained with volumetric titrations.

Calculations

Calculations are preceded by one assumption: that the weight of the sample collected is a reasonably accurate measure of volume, i.e., 50 mg. is equal to 50 μ l. Since the sweat is almost entirely water, the error accepted by this assumption is very small, less than the errors inherent in our weighing technique.

The data needed to calculate the concentration of chloride micro equivalents per unit

TABLE
Table of 10 Normals and 10 C/F
Variations of sweat chloride values in normal and cystic fibrosis
individuals as determined by pilocarpine iontophoresis sweat tests.

Patient	Meq Cl-/L on normal patients				Meq Cl-/L on C/F patients			
	Test No.				Test No.			
	1	2	3	4	1	2	3	4
1	5	6	6	6	87	87	78	92
2	4	5	5	6	89	98	93	100
3	9	8	5	7	113	115	117	123
4	10	12	15	16	75	77	63	66
5	20	20	21	23	71	101	110	119
6	9	9	10	11	62	89	97	118
7	8	8	8	11	92	74	97	110
8	5	7	7	6	93	100	98	89
9	12	16	16	17	102	108	129	129
10	6	7	8	10	110	114	120	105

Four consecutive sweat chloride determinations on 10 normal individuals and 10 patients with cystic fibrosis were done to illustrate normal variation of chloride values obtained from single individuals. Collections of the four sweat samples from each patient were made on the same day, within 4 hours of each other. All titrations of the samples from a single individual were done on the same day.

volume of the unknown sample have been determined above. They are: (1) the time required to titrate one micro equivalent of chloride, and (2) the time required to titrate the unknown number of micro equivalents of chloride in the collected samples.

The steps in the calculation are:

1. *Standard titration time* is the time required to titrate the blank plus the 1 micro equivalent of chloride minus the time required to titrate the blank.
2. *Unknown titration time* is the time required to titrate the unknown minus the time required to titrate the blank.

$$\begin{aligned} \mu\text{eq Cl in sample} &= \frac{1 \mu\text{eq Cl (in Stand.)} \times \text{Unknown Titration Time}}{\text{Standard Titration Time}} \\ \mu\text{eq Cl in sample} \times 100 &= \frac{\text{mg. of sample}}{\text{mg. of sample}} = \text{mEq/L of chloride} \end{aligned}$$

The chloride concentration of at least two of the three samples should agree within 10 mEq/L on normals and 20 mEq/L on C.F. patients (Table). Poor duplication suggests a need to do three more tests and to review collection techniques and analytical procedures.

Results

Since sweat chloride values are skewed to the right and do not form a normal curve, the simplest convenient arrangement for graphic presentation is the cumulative frequency curve, or ogive. The ogives in Figure 3 show the cumulative frequency distributions of sweat chloride values for three groups: 835 normal children under age 13, 105 patients with cystic fibrosis under age 13, and 216 normal individuals 13 and over. These sweat chloride determinations graphed in these ogives were done between January 1963 and July 1966. Similar ogives could be obtained for sweat sodium; however, they would be less satisfactory because the overlap of values from normals and patients with cystic fibrosis is much greater for sodium than for chloride.

It is essential that each hospital doing sweat tests establish its own range of sweat chloride

CUMULATIVE DISTRIBUTION OF Meq / L CHLORIDE
IN SWEAT ON 1,156 SWEAT SAMPLES
READ AS % LESS THAN

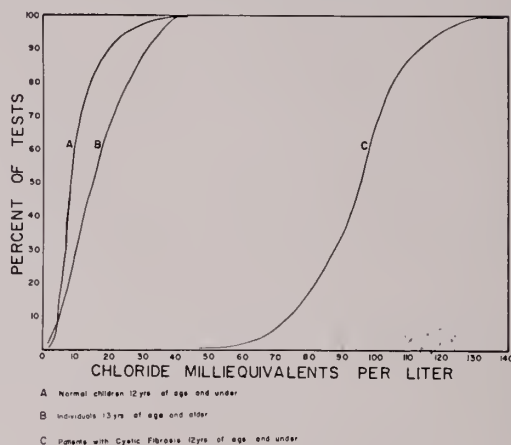


Fig. 3 — The above cumulative frequency distribution curves of sweat chloride concentrations are for three age groups: 835 normal children 12 years of age and under, 216 individuals 13 years of age and under, and 105 patients with cystic fibrosis 12 years of age and under.

The mean of those thirteen years and older is slightly higher than that of the 12 years of age and under group. There is a slight overlap of the upper 5 per cent of the normal group and the lower 5 per cent of the patients with cystic fibrosis.

values for normals and cystic fibrosis patients because slight differences in means and distribution of values exist from region to region. We believe these to be few due to variation in collection and analysis techniques; but other as yet unknown factors may be playing a role. A good ogive of normal or cystic fibrosis sweat chloride values can be established with 100 tests. During the period of data gathering, before establishing its own ogives, these ogives can be used.

Values in the lower 95% of the normal range may be considered diagnostic of normal; values in the upper 95% of the range for cystic fibrosis may be considered diagnostic of cystic fibrosis. Values in the upper 5% of the normal range and lower 5% of the cystic range should be reviewed with caution as a slight overlap occurs in this area. Patients whose sweat tests fall in this area should have repeated sweat tests and other diagnostic procedures such as duodenal intubation, analysis of sodium and potassium in nails, and lip biopsy.

References

1. Gibson, L. E., and Cooke, R. E.: A Test for Concentration of Electrolytes in Sweat in C/F of the Pancreas Utilizing Pilocarpine by Iontophoresis. *Pediatrics*, 23:545, 1959.
2. Cotlove, E., Trantham, H. V., and Bowman, R. L.: An Instrument and Method for Automatic Rapid, Accurate, and Sensitive Titration of Chloride in Biological Samples. *J Lab Clin Med*, 51:461, 1958.

Cartilaginous Tumors of the Larynx

Chondrosarcoma of the Larynx

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A MASS IN the neck, especially in the thyroid region, has often been considered a goiter, without much concern as to any other possibility. Because such a lesion may be of cartilaginous origin, the differential diagnosis in any case of a mass in the neck is important. The following is a report of a patient with this rare type of neck lesion who was recently seen at our clinic.

Report of a Case

A 73-year-old white woman was seen at the Mayo Clinic on August 26, 1963, because of a mass in her neck. The mass was located on the anterior right side (Figure 1) and was of approximately 10 years' duration. The patient had been well most of her life and implied to the examiner a very active and vigorous routine of daily living. She is still the sole owner and operator of a small-town dry-goods store, obtaining aid from no one, widowed for 16 years, and childless. One and one-half weeks prior to admission the patient admitted to having walked 1½ miles. Walking this distance was no strain for her at that time or previously. Her history was not significant; she could not recall having had any episodes of severe illness, and no surgery had been done. The patient is postmenopausal, with no reference to unusual difficulty during her "change of life."

Approximately 10 years before, she had noted a small mass about the right side of her neck, which she considered to be a goiter. About six years later the mass began to enlarge and continued to do so to the time of examination on August 26, 1963. The only difficulty the patient had noted with the mass was a coughing tendency with some choking, particularly when she was in the right lateral decubitus position. Dysphagia occurred late in the course of the present condition. The patient denied nervousness, easy fatigability, weakness, intolerance to heat or cold, sweating, dry skin, poor appetite, gain or loss of weight, aching, and palpitation. No medication (including iodine) had been taken.

Physical Findings

Physical examination revealed a well-developed, healthy-appearing, elderly lady with a large mass located about the anterior right side of her neck. The mass was huge and stony hard and was considered to be of thyroidal origin, measuring 12 by 10 by 8 cm. on the right, 8 by 8 by 8 cm. about the isthmus, and possessing at

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**Mayo Clinic and Mayo Foundation: Section of Surgery.

least two palpable nodules. Estimated weight was 500 Gm. The trachea was felt in the midline and grade 1 venous congestion and dilatation were noted about the right side of the neck. No bruit or stridor was detected, but minimal hoarseness was present. Neither eye signs nor changes in the skin, hair, or nails were noted and tremor was not present. The patient's blood pressure was 150/75. Her pulse rate was 72 beats/minute and regular in rhythm. Her temperature was 97.6 F.

Laryngoscopy was done and the report read, "Right cord fixed, false cord pushed to middle of larynx, right pyriform fossa full, all presumably from extension inwardly from a large goiter behind the thyroid cartilage."

Laboratory and X-ray Studies

Laboratory studies disclosed the following: Hemoglobin level, 11.7 Gm/100 ml.; erythrocyte count, 4,730,000/cu. mm.; leukocyte count, 5,500 cu. mm.; sedimentation rate, 24 mm. in 1 hour; blood group, B

(Rh —); Venereal Disease Research Laboratories test (VDRL), nonreactive; serum sugar, 64 mg/100 ml.; and protein-bound iodine, 5.4 μ g/100 ml.

Gammagram studies showed some uptake of iodine-131 to the left of the lesion, probably a consequence of palpable thyroid tissue in that region.

Roentgenograms of the chest showed evidence of calcification of the aorta and a large, 8-cm. soft-tissue mass just above the level of the clavicles displacing the trachea to the left, suggestive of goiter (Figure 2). Anteroposterior and lateral views of soft-tissue roentgenograms of the right side of the neck showed a 10-cm. round, soft-tissue mass in the anterior right side of the neck, containing large deposits of irregularly shaped calcium (especially laterally) and displacing the trachea to the left and back (Figure 3). The mass was presumed to be a goiter.

Surgery

The possibilities of adenomatous goiter with calcification, Riedel's struma, or carcinoma were considered before operation. At operation the mass was found primarily in the center of the neck and to the right, markedly displacing the right common carotid artery and the deep jugular vein to a point well lateral to the tip of the ear. Silverman needle biopsy revealed necrotic tissue. Much dissection was necessary before it was found that the mass was invading the thyroid cartilage and was actually arising above the thyroid gland. Laryngectomy was considered but not done. As much tumor as possible was removed; only a small 1.5-cm. region was left on the right side of the thyroid cartilage, which was evidently the origin of the mass. The thyroid gland itself was preserved. A No. 5 tracheostomy tube was put in place through the third tracheal ring in the midline.

Postoperative Course

An uncomplicated postoperative course followed. The feeding tube was removed on the tenth postoperative day, but the tracheostomy tube was retained because the patient had difficulty breathing when the tube was removed earlier. The patient was released from the hospital on the twelfth postoperative day. She was seen several days later at the clinic and was instructed to return in three to four months, at which time reevaluation would be necessary in addition to the possible removal of the tracheostomy tube.

Pathologic Diagnosis

The pathologic specimen from the laryngeal region weighed 430 Gm. and was a lobulated, semien capsulated grade 1 chondrosarcoma, 13 by 9 by 7 cm., with regions of central liquefaction (Figures 4 and 5). Attached to the lesion was a 10-Gm. portion of thyroid showing nonspecific thyroiditis.

Comment

Literature Review

Cartilaginous tumors of the larynx are rare.



Fig. 1 — Neck mass. Chondrosarcoma of larynx.



Fig. 2 — Roentgenogram of chest showing evidence of calcification of aorta and a large 8-cm. soft-tissue mass just above the level of clavicles, displacing the trachea to the left and suggestive of goiter.



Fig. 3 — Roentgenograms of the neck for soft tissues showing a 10-cm. round, soft-tissue mass in the anterior right side of the neck, containing a large amount of irregular-shaped calcium especially laterally (presumably a goiter) and displacing the trachea to the left and posteriorly. *A*, Anteroposterior view. *B*, Lateral view.



Fig. 4 — Surgical specimen from laryngeal region weighing 430 Gm. and lobulated, semien capsulated, grade I chondrosarcoma, 13 by 9 by 7 cm. with regions of central liquefaction. Note calcification throughout tumor.



Fig. 5 — Microscopic evidence of chondrosarcomatous changes. (Hematoxylin and eosin; x225.)

The first case was described in 1822 by Heusinger,¹ who classified these lesions grossly as "chondroides." Subsequently, similar lesions were discovered and described, and by 1961 with the publication of Hora and Weller bringing the total of recorded cases in the literature to 100.²⁻⁸

Twenty-two chondromatous laryngeal tumors were seen at the Mayo Clinic and reviewed in 1962 by Goethals⁹ working with Dahlin and Devine¹⁰; seven of these had been noted by New and Erich¹¹ in 1938 and were included in the previously mentioned 100 cases.

A more encompassing review of the literature was made in 1962 by Cocke,¹² who reported 136 cases of cartilaginous tumors of the larynx, referring to the studies of Gay and associates⁵ and of Hora and Weller.⁸ Seven of the 22 cartilaginous tumors reviewed by Goethals were included in New and Erich's¹¹ study; however, 15 were not included and are to be added for a total of 151 cases.

In the study of 136 tumors by Cocke, 130 were benign; six were malignant and were classified as chondrosarcoma. Of the 22 lesions reviewed by Goethals, 18 were low-grade chondrosarcomas and four were benign tumors.

In 1964, Rao¹³ reported a case of a laryngeal chondromatous tumor involving the epiglottis and classified the lesion as a chondroma.

To these (totalling 152), two additional cases of chondrosarcoma have been encountered at the Mayo Clinic since 1961, bringing the current total to 154. One of these includes the present case report.

Anatomical Features

Most of the reported chondromatous tumors

have developed on the endolaryngeal surface of the posterior plate of the cricoid cartilage, extending inward into the larynx. Lesions have involved other sites: namely, the pharyngeal (posterior) surface of the cricoid or lesions projecting from both surfaces, thyroid cartilage, and epiglottic and arytenoid cartilages. Growth has been found to be characteristically slow and expansile, causing pressure atrophy of contiguous structures and eventual involvement and obliteration of the normal laryngeal framework. Extrinsic growths have resulted in problems of deglutition, whereas intralaryngeal tumors have caused mechanical obstruction of the airway, with impeded movement of one or both vocal cords.

Ewing¹⁴ stated that chondromas usually form as solid, hard, lobulated, rounded tumors, which may attain large dimensions and may become softened by mucinous degeneration and cysts: the cysts are filled with serous, mucinous, or fatty material. Moore³ observed that these tumors usually are sessile and immovable and may be broad and flat, nodular, or irregular and are generally covered by a healthy or slightly hyperemic mucous membrane.

Lichtenstein¹⁵ and Lichtenstein and Jaffe¹⁶ established certain histologic criteria for the diagnosis of chondrosarcoma in cartilaginous tumors. These include richly cellular neoplastic tissue with (1) numerous cells with plump nuclei, (2) cells with multiple nuclei or hyperchromatism of the nuclei, (3) uninuclear giant cells, and (4) irregular-sized cells with irregular-sized nuclei. These criteria were also used by Dahlin and Henderson¹⁷ in their study of 212 chondrosarcomas.

Figi¹⁸ found that the average age for his six patients with laryngeal cartilaginous tumors was 52 years. In studying chondrosarcomas in other sites, Dahlin¹⁹ noted that they were more prevalent in the patients in the fifth and sixth decades, whereas Kragh and associates²⁰ noted an average age of 58.4 years. Males were more often afflicted. With cartilaginous tumors of the larynx, the ratio was approximately 4 to 1.

Slow Growth

Symptoms vary according to site, size, and rate of growth of the tumor, and usually are due to interference with deglutition or laryngeal functions, either respiratory or vocal, or both. Because the tumor grows slowly, onset is usually

insidious. Hoarseness, dyspnea, and the presence of an external neck growth are the usual order in which complaints are presented. In their comprehensive analysis of benign tumors of the larynx, New and Erich¹¹ noted that pain was infrequent and ulceration was extremely uncommon. Moore,³ New,²¹ and Figi¹⁸ found that hoarseness was usually the earliest symptom, with dyspnea the next most common complaint.

Typical laryngoscopic findings, as described by Moore,³ were those of a subglottic, large and round, projecting mass that was situated under one of the vocal cords and extended frequently to the midline of the larynx. Figi¹⁸ stated that the characteristic finding on laryngoscopy was a smooth, sessile^o mass covered with normal mucous membrane in which the blood vessels stand out prominently. Vocal-cord fixation, either partial or complete, may be present and may involve one or both cords. Various authors have described the appearance and examination of the tumor presenting on the external surface of the laryngeal cartilage as being fixed, smooth and hard, and without evidence of inflammation in the absence of glandular enlargement. The diagnosis, ultimately, is dependent on microscopic identification of a biopsy specimen despite the presumptive evidence of such a lesion from the history and laryngoscopic examination.

Roentgenography has proved beneficial, particularly in the presence of calcification, at which time it may be pathognomonic or very helpful when a definitely circumscribed tumor can be delineated.

Other mimicking benign tumors considered in the differential diagnosis, particularly when the lesion is subglottic, are: fibroma, fibrolipoma, angioma, neurofibroma, fibromyxoma, amyloid tumor, adenoma, and cysts of all types.

Treatment and Prognosis

Moore³ stated that the treatment for such growths is analogous to that for carcinoma in the same site and is operative. Prognosis for such patients has been favorable and survival has been relatively long, although local recurrences have commonly appeared after every type of surgical maneuver; recurrences have varied from one to 28 years after operation.

Summary

Chondrosarcoma of the larynx is an uncommon lesion that can simulate a goiter and should be considered in the differential diagnosis of any lesion of the neck. If the diagnosis is verified, the lesion should be treated adequately by surgical intervention. Prognosis with adequate therapy has been good despite local recurrence.

References

1. Heusinger, J. C.: System der Histologie, p. 91. Eisenach: J. F. Bäcker, 1822.
2. Alexander, Arthur: Die Knorpelgeschwülste des Kehlkopfes. Arch f Laryng u Rhin 10:181, 1900.
3. Moore, Irwin: Cartilaginous Tumours of the Larynx: A Study of All Recorded Cases. J Laryng 40:9; 84; 145, 1925.
4. McCall, J. W., Dupertuis, S. M., and Gardiner, F. S.: Chondroma of the Larynx: Review of the Literature and Report of Two Cases. Laryngoscope 54:1, 1944.
5. Gay, B. B., Jr., Wilkins, S. A., Jr., and Engels, E. P.: The Roentgenologic Characteristics of Chondroma of the Larynx. Amer J Roentgen 80:987, 1958.
6. Walter, W. L.: Chondroma of the Larynx: Report of a Case and a Review of the Literature. Ann Otol 68:1144, 1959.
7. Reinhard, M.: Die Knorpelgeschwülste des Kehlkopfes und Ihre Behandlung. Beihefte z Ztschr f Hals-, Nasen- u Ohrenh 8:121, 1960.
8. Hora, J. F., and Weller, W. A.: Laryngeal Chondroma. Arch Otolaryng 74:67, 1961.
9. Goethals, P. L.: Cartilaginous Tumors of the Larynx. Thesis, Graduate School, University of Minnesota, 1962.
10. Goethals, P. L., Dahlin, D. C., and Devine, K. D.: Cartilaginous Tumors of the Larynx. Surg Gynec Obstet 117:77, 1963.
11. New, G. B., and Erich, J. B.: Benign Tumors of the Larynx: A Study of Seven Hundred and Twenty-Two Cases. Arch Otolaryng 28:841, 1938.
12. Cocke, E. W., Jr.: Benign Cartilaginous Tumors of the Larynx. Laryngoscope 72:1678, 1962.
13. Rao, A. B. N.: A Case of Chondroma of the Epiglottis. J Laryng 78:315, 1964.
14. Ewing, James: Neoplastic Diseases: A Treatise on Tumors. 4th ed., pp. 1160. W. B. Saunders Co., Philadelphia, 1940.
- 15-21. May be secured from the author or the reprints.

Few people think more than two or three times a year; I have made an international reputation for myself by thinking once or twice a week.

—George Bernard Shaw

Paleolithic Man's Endurance Test

Primitive man was close to nature, but the fallacy of his medicine was its interference with nature. He regarded health and disease as a constant conflict between good spirits and bad spirits, each battling for victory.

The sick person was thus denied rest and quiet, for the disease-demons must be allowed no peace: they must be frightened away by terrifying masks and grimaces; by strange howls, noises, dances; they must be made uncomfortable by beating, biting, pinching, kicking, strangling their host; they must be smoked out by unbearable smells and fumigations. If they were strong enough to endure all this, then by sorcery they must be lured elsewhere, to take their abode in some scapegoat—an animal, or the patient's enemy, or an inanimate object. If they were too clever to be fooled, then they must be appeased with sacrifices and precious gifts. The medicine-man's treatment was so heroic that often he looked as ill and gaunt as his patient, but he never gave up. Even when the struggles of the patient ceased and the soul left his body, the medicine-man would try to blow it back through the various orifices—the mouth, the ear, the anus. Many patients died in their prime, but this merely meant that the demons had conquered—perhaps the deceased had been disrespectful. On the other hand, the medicine-man had many remarkable cures to his credit, and if he kept testimonials, his medicine-bag must have been full of them. In primitive medicine, as in modern, the patient's faith and the physician's personality are important factors in the cure, and often both are the victims of ignorance and suggestion.*

* Victor Robinson: *The Story of Medicine*, 1931.

Medical Men on Postage Stamps

Karl von Rokitansky (1804-1878) Austrian pathologist and pioneer in the science of pathological anatomy, was the first to detect bacteria in the lesions of malignant endocarditis, the first to distinguish between lobar and lobular pneumonia, and the first to describe spondylolisthetic deformities in his study of obstetrics and orthopedics. He also left a classic account of the pathological appearance of the liver in acute yellow atrophy. For his contributions to medical science Austria honored him on a postage stamp issued in 1954.

Jacques Daviel (1693-1762) was a French oculist credited with performing the first cataract operation in 1753. In recognition of his pioneer feat France issued a commemorative postage stamp in 1963.

Accommodating

The patient complained bitterly, "Five dollars is a lot of money for pulling a tooth—just two seconds' work."

"Well," replied the dentist consolingly, "if you wish, I can pull it very slowly."

California Encephalitis

Five
Cases
in
Southeastern
Minnesota

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EACH SUMMER AND fall physicians practicing in the Mississippi River valley area in Minnesota are faced with a difficult problem in the differential diagnosis of illnesses caused by enteroviruses and arthropod-borne viruses. During July, August and September of 1966 Winona, Minnesota, suffered an epidemic of encephalitis. The illness was most often seen in children. Five children who were observed by the authors had a clinical course and laboratory studies specific enough to identify their disease as California virus encephalitis. Prior to 1966 only four cases had been reported in Minnesota. The large number we observed probably represents increased awareness of the presence of this virus and vector^{oo} in Minnesota and improved availability of diagnostic tests rather than increased incidence.

The virus was isolated in 1943 in Kern County, California.^{2,5} It was first thought that the disease did not often extend to man or over a very large area, but later the virus was searched for and found in rabbits, rodents, and squirrels over a wide portion of the West Coast and southern Canada.³ Subsequent studies demonstrated that it can be endemic in character and that several species of mosquitoes are capable of the vector role.^{4,5}

The first recovery of the etiological virus from a human in the United States was made in 1964 from the fatal case of a child who had lived in the Winona section of the Mississippi River Valley. This strain of the virus (there are variations described within the California group) has been labeled the LaCrosse strain. Its isolation was unique in that four years elapsed between the first unsuccessful and the recent successful attempt. The brain had been stored at -40C. during the interval.⁶ A 1963 survey in Wisconsin found that persons carried the antibodies in direct proportion to the time they spent out-of-doors. Although the sampling used in that study

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**See Test Your Word Score Page 1227.

We are indebted to Dr. W. H. Thompson, Department of Public Health and Hygiene, Madison, Wisconsin, for the determinations which elucidated the virus.

was state-wide, groups tested from the western sections of Wisconsin had a higher rate of reactions.⁷

Diagnostic Criteria

A person is presumed to have been infected with the California encephalitis virus if any one of the following criteria is demonstrated: (1) isolation of virus; (2) a fourfold rise in hemagglutination-inhibition, antibody titer or complement fixation, titer between acute and convalescent specimens; (3) a fourfold fall in hemagglutination-inhibition complement fixation titer between acute and convalescent specimens; (4) a rise in neutralization index of 1.7 logs or greater. The category of presumptive cases was based on significant antibody in a single serum specimen; hemagglutination inhibition equal to or greater than 320, complement fixation equal to or greater than 8, or a neutralization index equal to or greater than 2.0 logs.¹

Case Reports

Case 1

This seven-year-old boy was admitted to Winona Community Memorial Hospital on August 8, 1966, with the complaints of severe headache, fever and irritability for two days. His parents reported that his development and school progress were "slow" and that he had had a "prolonged" febrile seizure at age four-and-one-half years. There was a minimal infection of the pharynx; otherwise no foci of infection were noted. His temperature was 103 degrees. Nuchal rigidity appeared on the second hospital day and a spinal tap revealed twenty cells, all of which were lymphocytes. The sugar was 47mgm.% and the total protein 28 mgm. His urine examination was normal.

He was treated for two days with chloramphenicol 20 mgm/kg. and procaine penicillin 1,000,000 units each day. During this interval he developed a transitory weakness of his left arm and hand as well as periods of mental confusion. These symptoms cleared, his need for sedation diminished, and his temperature became normal on the fourth day. He was discharged on August 16; reexaminations on August 30 and November 10 revealed no sequelae. The following is his serologic report:

Complement-fixation titer	September 10	October 3
Mumps	negative	negative
Western equine enceph- alomyelitis	negative	negative
California enceph- alitis	8/10	8/30
HI titer	1:20	1:20
C. F. titer	1:4	1:16

Neutralization (logs)
greater than 3:2

Tests for Eastern, Western, St. Louis, and Powassan encephalitis were negative.

Case 2

This four-year-old boy entered the local hospital on September 9, 1966, complaining of headache and vomiting. On the day prior to admission he was seen in the Winona Clinic because of vomiting and low-grade temperature (100.4). "Vesprin" (trifluoromazine hydrochloride) four mgm. in divided doses was given; however, the vomiting and cephalgia increased. The temperature was 101.4R on admission and nuchal rigidity was present. The urinalysis was normal. The initial hemogram revealed a hemoglobin of 11.8 Gm.; wbc. 13, 550; hematocrit 34%; differential, 73 segs. 5 bands, eosinophil, 19 lymphocytes and 2 monocytes.

The child's vomiting subsided and no intravenous fluid therapy was required. The temperature fell to normal on the fourth hospital day. He ate well after the second hospital day and played without evidence of neurological impairment. Reexamination on October 3 revealed no sequelae. The serologic report is as follows:

Complement-fixation titer	September 10	October 3
Mumps	Negative	Negative
Western equine enceph- alomyelitis	Negative	Negative
California enceph- alitis	9/10	10/3
HI Titer	less than 1:10	1:40
C. F. titer	less than 1:4	1:16
Neutralization (logs) greater than 3:3		

Serologic tests for Eastern, Western, St. Louis, and Powassan encephalitis were negative

Case 3

This nine-year-old boy complained intermittently of a headache for a week prior to his admission on September 26, 1966. On the day prior to hospitalization a marked photophobia accompanied by vomiting developed. His temperature was 101.2R at the time of his initial examination. Nuchal rigidity was present. The urinalysis was normal. The hemogram was as follows: a hemoglobin of 12.9 Gm., wbc. 22,850; hematocrit 37%, differential: segs. 71, bands 6, basophils 1, and lymphocytes 22.

The vomiting was intermittent during the first two days but not severe enough to pose a hydration problem. The headache and photophobia subsided during the first three days. He was discharged on October 1 and reexamined on October 20. No sequelae were noted. The patient's serologic report is as follows:

Complement-fixation titer for	September 28	October 20
Mumps	1:8	1:8
Western equine enceph- alomyelitis	negative	negative
California enceph- alitis	9/28	10/20

CALIFORNIA ENCEPHALITIS—JOHNSON AND ROGERS

HI titer	1:10	1:20	1:20
C. F. titer	1:4	1:16	1:16
Neutralization (logs) greater than 3:2			
Serologic tests for Eastern, Western, St. Louis, and Powassan encephalitis were negative.			
No virus was isolated from a stool specimen collected on September 9.			

Case 4

This five-year-old girl began complaining of a headache and photophobia on September 26, 1966. Two days later she began to vomit and was brought to the Winona Clinic. Her temperature was 100.4 degrees and a slight nuchal rigidity was noted. It was decided to observe the child at home; the mother is the night supervisor at our local hospital. The vomiting quickly subsided and she became afebrile on the fifth day. The headache improved, but the child continued to exhibit stiffness and soreness of the back. There was no tripod positioning; she was able to accomplish the "kiss the knee" test without drawing her knees up or showing hamstring tightness. A stool culture for virus isolation was negative. She was mildly confused for three days and photophobia persisted for ten days. At the end of the second week she resumed her normal play activities. Reexamination on October 19 revealed no residua. The serologic findings are as follows:

Complement-fixation	September 28	October 19	
Mumps	negative	negative	
Western equine encephalomyelitis	negative	negative	
California encephalitis	9/28	10/19	11/11
HI titer less than	1:10	1:10	1:10
C. F. titer less than	1:4	1:16	1:32
Neutralization (logs) greater than 3:2			
Serologic tests for Eastern, Western, St. Louis, and Powassan encephalitis were negative.			

Case 5

This twelve-year-old boy was admitted to the hospital on August 28, 1966, with a four- to five-day history of headache, vomiting, and malaise. He complained of some abdominal discomfort. The child's temperature was 99.6 degrees; no foci of infection were seen and no nuchal rigidity was noted. The urinalysis was normal. The hemogram was as follows: 14 Cm. hemoglobin, wbc. 15,650 with a differential of 82 segs., 1 basophil, 11 lymphocytes and 6 monocytes. The urinalysis was normal. On 8/29 the wbc. was 10,550 with a normal differential. The vomiting persisted and he received intravenous fluids for the first twenty-four hours. A nuchal rigidity was noted on August 30, and a spinal tap produced 17 cells, all lymphocytes. The culture was sterile. A stool culture for viral growth collected on the 31st was negative. The headache persisted for four days, then subsided without evidence of neurological impairment. He was discharged on September 2, and reexamined on September 9 and October 28th. No residua were noted. The serologic results are as follows:

Complement-fixation titer	August 31	November 17
Mumps	negative	negative
Western equine encephalomyelitis	negative	negative
California encephalitis		
HI titer	1:10 less than 1:10	
C. F. Titer	1:4	1:8
Neutralization (logs) greater than 3:7		
Serologic tests for Eastern, Western, St. Louis, and Powassan encephalitis were negative		

Discussion

The reporting of California encephalitis has been increasing rapidly during the last four years. The United States *Encephalitis Surveillance* report of the Communicable Disease Center records one case in 1963, 42 cases in 1964, and 59 cases in 1965. The annual summary for 1965 attributes three cases of arthropod-borne encephalitis to Minnesota. Two of these were Western equine encephalitis with one fatality. The third individual had California encephalitis and recovered.^{1,8}

The symptom complex of vomiting, fever, headache, and lethargy found most commonly in this entity is non-specific. A large group of central nervous system pathogens present a similar picture. However, California encephalitis is rare over the age of twenty.⁹ Photophobia can occur in encephalitis from many causes. In two of our cases, however, it was a striking finding. California virus encephalitis is usually a mild disease. All the patients reported here recovered without residual neurologic damage, motor, emotional or mental.

The definitive diagnosis is isolation of the specific virus or an appropriate rise in the antibody titer. Several species of mosquitoes have been found capable of carrying viruses of the California group. Of these *Culex tarsalis* was identified at the farm home of Case 4.¹⁰ *Culiseta inornata*, another vector, is also found in Minnesota. Birds have not been implicated in the role of host, but the small animal reservoir is large and includes rabbits and ground squirrels, which are abundant.⁹

Winona is built on an island of the Mississippi River. High water in the spring and early summer creates poorly drained ponds which afford

good mosquito-breeding sites. The vector population rises several weeks later and the potential exists for an epidemic.

The mildness of the symptoms, their non-specificity and the ease with which these five cases were discovered once diagnostic tests were obtained suggests that in terms of numbers of cases the California encephalitis virus may be an important central nervous system pathogen.

The Minnesota Department of Health plans to offer the specific serologic tests upon request to physicians who suspect a patient to have California encephalitis.¹³ We expect that a high index of suspicion and liberal use of these tests will find many children with the disease.

Conclusion

The five cases of California-virus encephalitis presented showed the usual mild form of the disease.

The recovery of the virus in 1964 from a pa-

tient who lived in southeastern Minnesota, the frequency of high antibody titers in southwestern Wisconsin, the annual late summer-early fall appearance of sickness in children associated with central nervous system symptoms, and the identification of the virus by indirect means in these five cases suggest that this part of the Mississippi River valley is an endemic region.

Families should be informed about the increased hazard of mosquito bites in this area so that appropriate family and individual control measures can be taken.

Although specific therapy is lacking, awareness of the mild clinical course dictates watchful waiting and enlightened supportive therapy.

ACKNOWLEDGMENT

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References

1. Communicable Disease Center. Encephalitis Surveillance, Annual Summary 1934.
2. Hammon, W. McD., Reeves, W. C., and Sather, G.: California Encephalitis Virus, A newly Described Agent. II. Isolations and Attempts to Characterize the Agent. *J Immun* 69:493, 1952.
3. Newhouse, V. F., Burgdorfer, W., McKiel, J. A., and Gregson, J. D.: California Encephalitis Virus. Serologic Survey of Small Wild Mammals in Northern United States and Southern Canada and Isolation of Additional Strains. *Amer J Hyg* 78:123, 1963.
4. Gresikova, M., Reeves, W. C., and Scrivani, R. P.: California Encephalitis Virus: An Evaluation of its Continued Endemic Status in Kern County, California. *Amer J Hyg* 80:229, 1964.
5. Reeves, W. C., Hammon, W. McD.: California Encephalitis Virus, A Newly Described Agent. Mosquito Infection and Transmission. *J Immun* 77:303, 1952.
6. Thompson, W. H., Kalfayan and Anslow, R. O.: Isolation of California Group Virus from a Fatal Human Illness. *Amer J Epid* 81: 2: 245.
7. Thompson, W. H., and Evans, A. S.: California Encephalitis Virus Studies in Wisconsin. *Amer J Epid* 81:230, 1965.
8. Communicable Disease Center. Encephalitis Surveillance, Annual Summary, 1964.
9. Crumblett, H. G., Stegmiller H. I., and Spencer, C.: California Encephalitis Virus Infection in Children. *JAMA* 198:108, 1966.
10. Zwonitzer, R. L., Asst. Prof. Biol., College of St. Teresa, Personal communication.
11. Hammon, W. McD., and Reeves, W. C.: California Encephalitis Virus. *Calif Med* 77:303, 1952.
12. Lennette, E., Magoffin, R. L., and Knouf, E. G.: Viral Central Nervous System Disease. *JAMA* 179: 687, 1962.
13. Nelson, C. B., Chief Section of Acute Communicable Diseases, Minn. Dept. of Health. Personal communication.
14. Likar, M., and Casals, J.: Isolation from Man in Slovenia of a Virus Belonging to the California Complex of Arthropod-Borne Viruses. *Nature*, 197: 1131, 1963.

The longer I live the more keenly I feel that whatever was good enough for our fathers is not good enough for us.—Oscar Wilde

Hat: something the average man covers his head with, the beggar passes around, the statesman throws into the ring, and the politician talks thru.

Viking

The Typical, Atypical, and "Atypical" Ductus Arteriosus

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SIXTY YEARS AGO in an address before the Philadelphia Academy of Surgery Dr. John Munro, a Boston surgeon, made a strong plea for the clinical application of ligation of the patent ductus arteriosus.¹ Although his message was published in the *Annals of Surgery* in 1907, it went unheeded, as his medical colleagues never referred to him a patient with a patent ductus arteriosus for surgical closure.

Thirty years ago on March 6, 1937, another Boston surgeon, Dr. John Streider, attempted unsuccessfully to suture ligate a patent ductus arteriosus in a woman with bacterial endocarditis.⁴

One year later at the Boston Children's Hospital Doctor Gross, unaware of Doctor Streider's attempt, did successfully perform the first ligation of a patent ductus arteriosus and entered a new era in cardiac surgery.² Five years later Doctor Gross reported 14 successful cases of division and suture of the ductus arteriosus and recommended this technique as superior to ligation alone.³

Incidence

Statistically, patent ductus arteriosus is a very important lesion and, of the cardiac lesions in the infant, ought to be the third most common, following ventricular septal defect and tetralogy of Fallot.

Etiology

An etiologic association with German measles in the first trimester has been made as well as an association with high-altitude living in Peru. A dominance in females is well recognized and a familial inheritance has now been reported several times.⁵

Anatomy and Physiology

In intra-uterine life blood reaches the descending aorta from the pulmonary artery through the

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fetal communication of the ductus. Embryologically, the ductus originates from the dorsal part of the sixth branchial arch and, although a branch of the left pulmonary artery, the general contour of its course conforms with that of the main pulmonary trunk.

Experimental observation indicates that anatomic closure of the ductus begins during the last weeks of intra-uterine life and continues for several weeks after birth. Normally it closes functionally with the increase in the oxygen of the fetal blood and the lowering of the pulmonary arterial resistance with the first respirations. Subsequently the ductus undergoes fibrosis and remains as a ligament leading to an interruption of the flow of blood. If it remains patent, there is a reversal of the flow and a persistence of the patent ductus arteriosus.

With the increasing use of cardiac catheterization in the late 1940s and early 1950s many patients with open ductus arteriosus were diagnosed, though they were not recognized clinically because of the absence of the typical murmur and the other usual signs of a patent ductus arteriosus. These seemed to occur in very sick children with markedly elevated pulmonary artery pressures from birth which altered the hemodynamics of the shunt, changing the degree of turbulence of flow and thereby the characteristics of a typical murmur, this group constituting the "atypical ductus arteriosus." In addition to these two, there is a group of cardiovascular defects producing systolic-diastolic murmurs which mimic the murmur of patent ductus arteriosus.

The Typical Patent Ductus Arteriosus

Diagnostic Features

Most of the children with the classical, simple, or typical patent ductus arteriosus are asymptomatic, and attention to the defect is made by discovery of the classical murmur in the left 2nd intercostal space. However, a few suffer from recurrent severe respiratory infections, underdevelopment, and easy fatigability. Cyanosis or clubbing^o is never present.

A thrill, systolic or systolic-diastolic, is often noted. Left chest prominence is common and the cardiac impulse is hyperdynamic at the apex. A wide pulse pressure with bounding peripheral

pulses may characterize the large extracardiac left-to-right shunt.

The prominent diagnostic feature, however, is the *murmur* described as the "train in the tunnel" or "continuous roaring," or "continuous machinery" murmur best heard in the left upper sternal border and radiating out along the second intercostal space. The murmur is constant, varying little with breathing or position. It is to be differentiated from other systolic-diastolic murmurs heard precordially, of which the most common deceiver is the so-called venous hum.

A typical machinery murmur or frequently any murmur is very rarely heard at birth in infants with patent ductus arteriosus. The exception is the premature infant. Even if a murmur is recognized or discovered in the first few weeks of life, it is seldom labeled as a continuous one. Most often only a systolic component is heard, probably because only a systolic gradient exists between the two circuits. This may be related to persistence of the fetal type of pulmonary arterial bed. Six to twelve months later, however, in most patients with typical patent ductus arteriosus the characteristic murmur is noticeable.

Procedure Studies

The findings on chest x-ray depend on the magnitude of the left-to-right shunt through the patent ductus arteriosus. A normal cardiac shadow may be present with a small patent ductus arteriosus. In larger shunts, left atrial and left ventricular enlargements are visible, as is a large ascending aorta and aortic arch, prominent pulmonary artery, and pulmonary vascular engorgement.

The electrocardiogram, like the chest x-ray, may be normal in patients with a small patent ductus arteriosus. With a large shunt the increased left ventricular flow work is reflected in left ventricular hypertrophy. Left axis deviation is present in 10 percent of the patients. Vector cardiography is usually consistent with left ventricular hypertrophy.

Cardiac catheterization is not usually necessary in making a diagnosis of typical patent ductus arteriosus. When it is performed, the catheterization should show an increase in arterial oxygen saturation of at least 6 percent in the blood of the pulmonary artery as compared with that in the right ventricle. These studies demon-

*See Test Your Word Score Page 1227.

strate that the pulmonary artery or right ventricular pressures are normal in more than 75 percent of the patients who have a patent ductus arteriosus. The pulmonary vascular resistance is normal in at least 90 percent. The pulse pressure is wide and left atrial pressure is slightly elevated. The pulmonary-systemic flow ratio is more than 1.5:1.0 and occasionally may be as great as 6:1. The catheter may be manipulated across the ductus in a majority of the patients, especially infants. Once through the ductus the catheter usually takes a sharp downward course along the descending thoracic aorta. This is in marked contrast to other aorto-pulmonary shunts such as a truncus or aortic-pulmonary window where the catheter usually ascends. If the catheter after going through the ductus should course upward, a lateral or left anterior oblique projection is able to differentiate from the latter two conditions.

Forward angiography has not been very helpful in differentiating patent ductus arteriosus from other L-R shunts. Retrograde aortography, however, is quite valuable not only in demonstrating the presence of a ductus but in estimating its degree of patency and the size of its shunt.

Complications

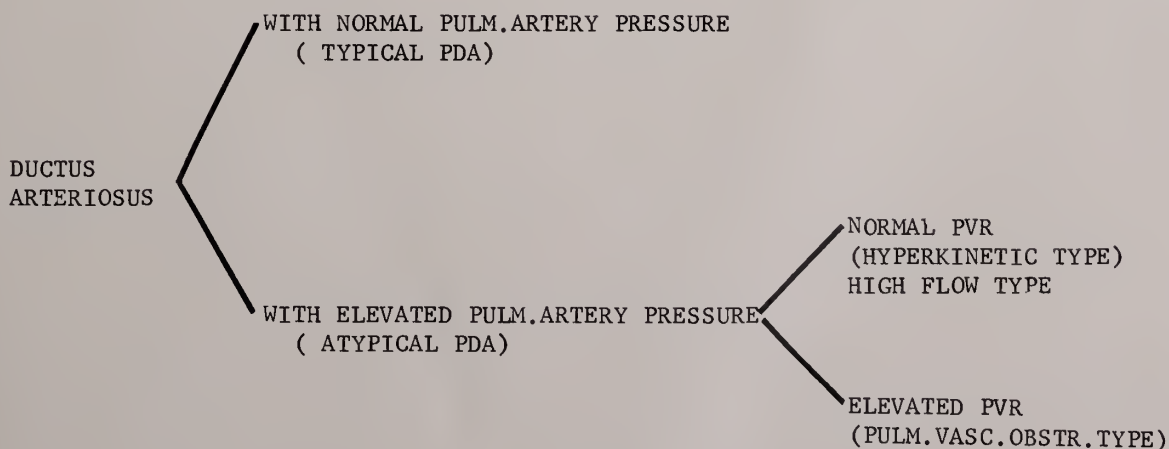
The complications of an unattended patent ductus arteriosus are pulmonary vascular hypertension, congestive heart failure, and bacterial endocarditis. The average patient with this anomaly is nearly asymptomatic throughout childhood. Later when the patient reaches the 20s and 30s, fatigue and breathlessness become in-

creasingly noticeable and congestive failure ensues. A very small patent ductus arteriosus may remain asymptomatic throughout life.

Treatment

The treatment for the typical patent ductus arteriosus is surgical closure. Most cardiologists recommend the operative closure for every child with this condition for two main reasons. One is the unlikelihood that the patient without surgery will be able to live a symptom-free life for the average length of time and the other is that normal circulation is completely restored by surgery with a very low mortality.

Initially, the recommended age for surgery was between three and 15 years of age. In recent years surgery is recommended earlier not only for the symptomatic patient but for the asymptomatic as well. If the team in the community, including cardiologist, anesthesiologist, and pediatric nursing personnel as well as the surgeon, are well acquainted with cardiac surgery in small infants, then a policy of treating patent ductus arteriosus surgically when it is first encountered is not only possible but advisable. Early surgery within the first two years of life and frequently within the first year of life is often mandatory in the patients who are sick. In the asymptomatic infant early surgery relieves the over-work burden on the left ventricular myocardium and may reverse pulmonary vascular changes, and if it can be demonstrated as a safe operative procedure, then it is advantageous to perform it early.



Figure

Postoperatively, the heart diminishes in size, pulse pressure becomes normal, electrocardiographic and radiologic evidence of left ventricular hypertrophy disappear, and pulmonary vasculature becomes normal. In most individuals, if the murmur is not gone by the time the patient leaves the hospital, any residual systolic murmur will have disappeared within the first year after surgery.

The Atypical Ductus

The atypical ductus child is the child with elevated pulmonary arterial pressures from birth. This is in contrast to those occasional typical ductus patients who develop elevated right-sided pressures later in life.

Although children with the typical ductus can be in trouble early in life with left ventricular overflow leading to congestive failure in infancy, these children constitute a minority of the large group of typical patent ductus arteriosus patients. On the other hand, a child with an atypical patent ductus arteriosus *as a rule* is a sick child and physiologically falls into one of two groups (Figure).

The first group is made up of infants with large patent ductus, tremendously increased pulmonary blood flow, and normal or only slightly increased pulmonary vascular resistance. A systolic murmur is heard best at the 2nd to 3rd left interspace and an early diastolic murmur is also heard frequently but, when present, forms a to-and-fro murmur rather than a continuous one. These children, like those with large ventricular septal defects, have a stormy infancy with attacks of pneumonia, pulmonary edema, and congestive failure. This difficult period is followed by a relatively symptom-free childhood. Not until later in adolescence does pulmonary vascular obstruction occur with reversal of shunt, cyanosis, and death.

The second group is made up of patients with only a moderate-sized ductus with pulmonary vascular obstruction. These children are cyanotic from birth. They are small, thin, and scrawny. Their auscultatory findings are the least typical. Their electrocardiogram shows pure right ventricular hypertrophy, and cardiac catheterization demonstrates pulmonary vascular resistance equal to or higher than systemic resistance.

The chest x-ray in atypical ductus always demonstrates or portrays gross abnormality. Right

ventricular enlargement is present in addition to the left, as is usually seen with typical patent ductus arteriosus. The pulmonary artery is prominent as usual. In many advanced cases of the pulmonary vascular obstructive type the peripheral lung fields may be ischemic in contrast to and accompanying the engorged hilar vessels.

Dr. Glen Cayler has shown a good correlation between an electrocardiogram and the pulmonary artery mean pressure in infants with ductus.⁷ Pure right ventricular hypertrophy is always associated with a mean pressure greater than 50 mm. of mercury, and pure left hypertrophy is never associated with a mean pressure higher than 50 mm. of mercury.

Cardiac catheterization, mandatory in atypical patent ductus arteriosus, in addition to demonstrating the levels of the shunt, will point out the degree of pulmonary hypertension as well as the magnitude of the shunt and the nature of the pulmonary arterial bed. As mentioned for the typical patent ductus arteriosus previously, aortography or dye injected from the systemic side will demonstrate sharply the left to right shunt, while right to left shunts are well shown by pulmonary artery injection.

Treatment of Atypical Ductus

The outlook for patients with atypical ductus unattended can be summed up as that of progressive pulmonary vascular obstruction. However, the treatment of the atypical ductus patient cannot be summarized as easily as that for the ductus patient without pulmonary hypertension. The atypical ductus with high flow and normal pulmonary vascular resistance offers no problem in recommending surgical correction. Nadas⁶ feels that as the increased flow and pressure throughout the pulmonary bed are present during the entire cardiac cycle, progressive pulmonary vascular obstruction may occur sooner in infants with large patent ductus arteriosus than in those with large ventricular septal defects. In view of this possibility of progressive pulmonary vascular obstruction, operation, if it can be performed safely, is indicated as soon as the diagnosis is made.

The decision for surgical treatment of the child with high pulmonary vascular resistance is much more difficult to make. Without surgical intervention on the ductus these patients die at an early age. However, surgical closure involves a

high risk and the survivors may still carry the same established pulmonary vascular resistance which occasionally has been shown to increase to an even greater level postoperatively. Various plans of surgical management have been advised. One can summarize these by stating that if the calculated shunt is predominantly left to right, surgical closure is advised. If predominantly a right to left shunt (cyanotic), closure of the patent ductus arteriosus is contraindicated. In the border-line cases of near balanced shunting the surgeon constricts the ductus and watches the behavior of the heart and the pressure in the main pulmonary artery.

Imitators of Ductus Arteriosus

Many people feel that the diagnosis of typical patent ductus arteriosus at least beyond the age of infancy, should be made on clinical grounds alone. However, as mentioned earlier, other cardiovascular anomalies with systolic and diastolic murmurs in the vicinity of the second left interspace may mimic patent ductus arteriosus and may require differentiation. These are listed in the Table. A jugular venous hum is probably the most common deceiver. Specific differentiation of the characteristics of each defect is beyond the scope of the present report and the reader is referred to the appropriate pediatric cardiology text. One such case, however, that of an A-P Window, because of its anatomic and surgical similarity, is included with license in the present list of ductus cases. In view of its rare successful management by direct division and suture, this case has been reported in a separate communication.

Comments

The present report includes 25 consecutive

TABLE

The Imitators of Patent Ductus Arteriosus

Defects which mimic a ductus arteriosus with systolic murmur is in vicinity of the second left interspace.

1. Jugular venous hum
2. Aortopulmonary septal defect
3. Coronary arteriovenous fistula
4. Pulmonary arteriovenous fistula
5. Collateral arterial circulation
(Coarctation of aorta) (Tetralogy of Fallot)
6. Ventricular septal defects with aortic regurgitation.
7. Ruptured sinus of Valsalva
8. Truncus arteriosus

cases surgically treated. Forty-four percent were under the age of two and most were symptomatic, requiring attention at an early age. This prompted earlier diagnosis and surgery and led to the present thesis that surgery at an early age is just as safe as surgery performed later. It should also be noted that only three patients exhibited cyanosis and all three had associated cardiac defects. The typical murmur was heard in only 13 cases.

Only one chest x-ray was interpreted as being normal. Cardiac enlargement and increased pulmonary vascularity were common findings. Specific chamber enlargement in an infant is difficult to ascertain on a routine chest x-ray, but occasionally individual chamber enlargement was defined by the radiologist with the aid of cardiac fluoroscopy.

In order to separate the typical from the atypical ductus arteriosus the pulmonary artery pressure is a single test that will make this differentiation.

The results show that there was no mortality and no significant morbidity delaying the patient's discharge. Closed thoracotomy for recurrent postoperative pneumothorax was performed in one child. Six children showed systemic hypertension, usually of a mild degree for one to six days postoperatively. There were no wound infections. One child underwent right middle lobectomy for chronic bronchitis and bronchiectasis three years after closure of the ductus. Another child, listed as only a fair result, was extremely ill for as long as six weeks postoperatively in the hospital and 10 months later was still not gaining, weighing only 12 pounds, nine ounces. He probably represents the atypical ductus with high pulmonary vascular resistance, although the extent of resistance was never calculated.

Enthusiasm for the results is modified and listed as only very good in several cases by the remaining presence of associated defects or physical or mental limitations. As far as the ductus was concerned, the postoperative course of these patients was excellent.

Summary

The clinical features of typical and atypical patent ductus arteriosus have been reviewed and other cardiovascular defects simulating ductus clinically have been listed.

Earlier surgery for patent ductus arteriosus is strongly advocated not only to salvage the atypical patent ductus arteriosus patient from that large group of infants mortally condemned with cardiovascular defects in the first year of life, but in the typical ductus patient as well, so as to relieve the left ventricular myocardium of its overwork and to restore the pulmonary vascular bed to normal sooner.

Recognition of the defect mimicking ductus before surgery so as to plan a proper approach is demonstrated by a case of aorto-pulmonary fenestration.

A consecutive case series is presented to demonstrate the safety of such surgery in a ductus group with an unusually high percentage of infants of younger age.

References

1. Munro, John: Ligation of the Patent Ductus Arteriosus. *Ann Surg* 46:335, 1907.
2. Gross, Robert E. and Hubbard, J. P.: Ligation of Patent Ductus Arteriosus. *JAMA* 112:729, 1939.
3. Gross, Robert E.: Complete Surgical Division of Patent Ductus Arteriosus. Report of Fourteen Successful Cases. *Surg Gynec Obstet* 78:36, 1944.
4. Meade, Richard H.: The Story of the Development of Surgery for the Patent Ductus Arteriosus. *Surgery* 40:807, 1956.
5. Lynch, H. T., Grissom, R. L., Magnuson, C. R., and Krush, A.: Patent Ductus Arteriosus Study of Two Families. *JAMA* 194:135, 1965.
6. Nadas, Alexander S.: *Pediatric Cardiology*, 2nd Edition, W. B. Saunders Co. 1964.
7. Cayler, G. G., Ongley, P., and Nadas, A. S.: Relation of Systolic Pressure in the Right Ventricle to the Electrocardiogram. *New Engl J Med* 258:979, 1958.
8. Lynch, M. F., Katkov, Harold, Jensen, N. K., Peterson, C. A.: Successful Division Aorto Pulmonic Fenestration. In Press.

Rural Scholarship Pays Off*

Dear Dr. and Mrs. Sheppard,

My husband has gone to deliver our neighbor's first baby: one of his first patients.

As I sit here waiting anxiously for the results I was impelled to write and thank you for making this good life possible for both of us through the benefits of the Rural Scholarship which we accepted a few years ago. We so thoroughly appreciate what you have done to help get us started.

I know that there are other young women with doctor husbands who will soon be setting up practice in rural Minnesota as we have done. I know that some of these wives may have misgivings about leaving the city, and if I knew who they were, I would like to write to them to let them know what a wonderful life it is to be the wife of a general practitioner in this beautiful state of ten thousand lakes. Life is never dull and the people in a small town are delightful. They are truly interested in the worthwhile things in life and are wholly without the numerous tensions of a metropolitan center. I wish I could somehow encourage more young doctors and their wives to locate in one of these invigorating smaller cities of Minnesota where every day is filled with new and stimulating happiness.

Lorna Wing
Sleepy Eye, Minnesota

*This is a scholarship given to medical students by The Minnesota State Medical Association. \$1,000 each year for four years is given to the recipient of the scholarship with the stipulation that after a year's internship, the doctor will practice for five years in a rural area.

YOUR HEALTH—MR. PRESIDENT!

Theodore Roosevelt (1858-1919)

A kaleidoscopically changing pattern characterizes Theodore Roosevelt's health history—marked by novelty, frequency, and violence. No President, preceding or succeeding, met vulnerability to disease and accident with such cavalier invincibility.

In infancy and childhood young Teddy was pathetically puny and spindly, chronically asthmatic and croupy; host to measles, chickenpox, and mumps; and so congenitally myopic that he was never to dispense with thick-lensed spectacles: whence his sobriquet of Four-Eyes. When engaged in active military service in adulthood he always had available a reserve of 12 extra pairs of glasses to allow for breakage on the battlefield.

In 1884 incipient tuberculosis impelled the young man Roosevelt to go ranching in North Dakota, where he engaged in a rugged program of busting broncos, two of which threw him: one for a broken arm and the other for a broken scapula. Fractured bones notwithstanding, he gained enormously in stamina from his year in the Wild West: the year that marked his matriculation from the wan, frail youth into the Rough Rider.

In 1900, while in Colorado campaigning for the vice-presidency, Teddy was accidentally bumped on the chest by a large timber, with no more serious trauma, however, than a severe abrasion. But to him the merest scratch!

After Roosevelt became President his athletic predilections turned to boxing, and during one match his left eye was inadvertently grazed by the glove of his opponent, resulting in retinal hemorrhages followed by retinal detachment. His vision in that eye never returned.

In 1904 a toss from a horse landed the advocate of the strenuous life prone on the ground with such violent impact that his face was unrecognizable behind swelling, cuts, and bruises. Savagely jarred were his neck and shoulders; but no bones were broken, although it was feared for a while that his spine and skull might have been injured.

In 1908 a badly abscessed tooth was extracted.

In 1912, while in Milwaukee to make a speech, Roosevelt was shot in the chest but declined examination of the wound until later. Said he: "I'll make this speech or die." When he approached the lectern on the Auditorium stage and removed his notes from his inner pocket he found a hole bored right through them and blood on his shirt. But that observation failed to deter him from delivering his 90-minute speech in full and with gusto. On later examination of the wound three attending doctors made this statement: "Colonel Roosevelt has a superficial flesh wound below the right breast with no evidence of injury to the lungs. The bullet is lodged somewhere in the chest wall . . . Bleeding was insignificant and the wound was immediately cleaned externally and dressed with sterile gauze . . . As the bullet passed through Colonel Roosevelt's army overcoat, other clothing, doubled manuscript and metal spectacle case, its force was much spent."

On subsequent hospitalization Roosevelt noted meticulously all that was said at his bedside and reported to a friend: "There are only three possible dangers, pleurisy, pneumonia and blood poisoning; the bullet is relatively harmless, but the breaking of that rib might result in pleurisy or even lead to pneumonia, and blood poisoning is a possible late complication from infection of the wound." (In their report the doctors either neglected to mention a broken rib or failed to discover it until later.)

Continued

In 1913, while on a speech-making tour and nature exploration in South America, the Rough Rider was catapulted out of his canoe onto a sharp rock which gouged into his thigh, producing speedy infection, swelling and suppuration with ensuing abscess formations, which subsided temporarily only enough to allow him to continue his safari, about which he said in retrospect: "I had to go. It was my last chance to be a boy." Was he ever not a boy!

In 1918 Roosevelt was hospitalized for a recurring thigh abscess, inflammatory rheumatism, and otitis media in both ears. With medical treatment the right ear cleared up, but the infection in the left ear culminated in mastoiditis—for which no surgery was done and which left him permanently deaf in that ear.

On tour in the Middle West he developed erysipelas in one leg, which failed, however, to daunt his plans or halt his progress. Later, inflammatory rheumatism recurring, he was hospitalized for treatment and then released to retire to his home at Oyster Bay.

On January 5, 1919, the indomitable Teddy died in his sleep of a coronary embolus. He had once said: "Only those are fit to live who do not fear to die; and none are fit to die who have shrunk from the joy of life and the duty of life. Both life and death are part of the same Great Adventure."

With acknowledgements to Karl C. Wold, M.D.: Mr. President—How Is Your Health? and to William Davison Johnston: T.R., Champion of the Strenuous Life.

Ninth Annual Methodist Hospital Symposium

The ninth annual symposium, sponsored by the Methodist Hospital Staff will be held on Saturday, September 16, 1967 at the Methodist Hospital Auditorium.

The subject of this scientific session is "Rheumatoid Arthritis" and will include the following topics and speakers:

"Rheumatoid Factor and the Pathogenesis of Rheumatoid Arthritis"—Morris Ziff, M.D.—Dallas, Texas

Film: "Examination of Joints"—Part I—Paul J. Bilka, M.D.—Minneapolis, Minnesota

Film: "Examination of Joints"—Part II—Paul J. Bilka, M.D.—Minneapolis, Minnesota

"Basic Treatment Program"—Howard F. Polley, M.D.—Mayo Clinic, Rochester, Minnesota

"Drug Treatment: Steroids, Indocin and Antimalarials"—Charley J. Smyth, M.D.—Tucson, Arizona

"Orthopedic Aspects"—Adrian E. Flatt, M.D.—Iowa City, Iowa

The Minnesota Academy of General Practice has approved this symposium for 6 prescribed hours of credit.

Following the symposium, a dinner dance for all physicians and wives will be held at the Interlachen Country Club, beginning at 6:30 p.m. A charge of \$8.00 per person will be made for the dinner dance, and reservations are required. There is no registration fee for the scientific sessions or the noon luncheon.

All physicians are most cordially invited to attend. For additional information please contact any of the following physicians: David Randall, M.D.—929-4500; Harold Berris, M.D.—588-0661; Edward L. Segal, M.D.—929-1313.



Editorials

Acute Arterial Occlusion*

IN MOST CIRCUMSTANCES the diagnosis of acute arterial occlusion is not difficult. The finding of a cold, pale, pulseless extremity will alert most physicians that a medical emergency exists. Unfortunately, the clinical situation is not always clear-cut, and disastrous delays in carrying out the proper treatment may result.

Acute iliofemoral thrombophlebitis is not uncommonly confused with acute arterial occlusion. The swollen, pale limb seen in phlegmasia alba dolens** is usually quite tender to palpation, especially in the femoral triangle, and the skin is pale but not cool. The superficial veins are congested rather than collapsed as in arterial occlusion. Because of the associated edema and, more rarely, arterial spasm, pulses may be difficult to palpate; however, after a period of bed rest they usually become palpable. Pain may not be a prominent complaint in either disease. In fact, it is present in only about half of the patients with acute arterial occlusion. Muscular impairment is rarely seen in venous disease but is common in a limb severely ischemic after acute arterial occlusion.

Several points deserve emphasis. First of all, the examination and systematic recording of peripheral arterial pulsations should be a routine part of every physical examination, particularly

in elderly patients. This procedure will aid considerably in a more accurate diagnosis of acute arterial occlusion. Certainly, when a patient complains of pain or distress in an extremity, no matter how bizarre it may seem, prompt evaluation of the peripheral arterial pulsations should be carried out. Prompt diagnosis must continue to be emphasized because unnecessary delays will almost certainly result in the loss of a useful extremity.

During the initial period following acute arterial occlusion, conservative medical management, including the use of heparin, vasodilators, and careful protection of the involved extremity, has continued to be the fundamental means of treatment. Environmental but certainly not local heat is also a helpful maneuver in an endeavor to facilitate vasodilatation. During this time the patient's general medical status can be evaluated for evidence of underlying cardiac disease, such as mitral stenosis or recent myocardial infarction, as a possible source of peripheral emboli. If evidence of significant ischemia persists after several hours of conservative treatment, surgical repair should be attempted, provided the patient's general medical status is reasonable, and even if it is far from being optimal. Advances in surgical technique, including the development of the Fogarty catheter, have made surgical inter-

Continued

*Gregg, Robert O.: Acute Arterial Occlusion in the Lower Extremity. *Minnesota Med* 49:1835, 1966.

**See Test Your Word Score Page 1227.

There are 36,700* undetected diabetics in Minnesota

Most of these are probably among patients over 40; the overweight; relatives of diabetics, and mothers of large babies. By the time polyphagia, polyuria, polydipsia, pruritus or other overt symptoms of diabetes appear, damage may have been done that could have been minimized. DEXTROSTIX® gives you a reliable blood-glucose estimate in 60 seconds.

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*Based on Statistical Report, U.S. Dept. Commerce, ed. 86, and Fisher, G. F., and Vavra, H. M.: Pub. Health Rep. 80:961 (Nov.) 1965.

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vention in acute arterial occlusion much more feasible and effective. Even in the high-risk surgical patient, the arterial occlusion may be corrected and a viable and, even more important, a functional limb may result. In the present-day management of acute arterial occlusion, the sal-

vage of a viable but severely ischemic, painful, and useless extremity can no longer be considered a good result.

Gerald J. Kavanaugh, M.D.
Rochester, Minnesota

Wringer Injuries^{*}

UNFORTUNATELY THE gradual demise of the electric washing machine wringer does not herald the disappearance of the wringer injury. Severe roller-crush injuries are also well-recognized hazards of road and factory accidents. The "ringer foot" is seen when an automobile tire passes over and crushes a foot into soft turf. As in wringer injuries of the hand, initial findings may be minimal and the patient is often sent home without treatment. Because of the foot's dependent position, swelling may progress rapidly and to alarming proportions. Proper immediate treatment is a compression dressing to include the toes and elevation. Partial weightbearing should not be allowed until dependent edema and pain are no longer a problem.

The number of mangle injuries of the hand has increased over the years as more and more homes have become equipped with ironers. These mangles consist of a rolling mechanism and a cast-iron shoe. In this type of injury a profound burn, often third degree, is added to the mechanical trauma of the roller. In very severe cases amputation of digits may occur.

Heavy steel and rubber rollers are not uncommonly found in industrial plants. Mechanized conveyor belts are the very essence of "mass production." Wheels, belts and pulleys are necessary and intrinsic to heavy machinery and, although usually guarded and fenced, a stray finger or hand is never far away. All are capable of

producing crushing injuries which are duplicates or slight modifications of the typical wringer injury.

Reducing edema has always been of immediate importance in the treatment of wringer injuries. This fluid seeps into and around muscles, tendons and ligaments and is gradually replaced by fibrin strands. Eventually connective tissue is laid down and permanent limitation of motion occurs. Sterling Bunnell's maxim, "Edema is glue," is especially appropriate here. In addition to compression and elevation, stellate ganglion blocks to reduce edema have been suggested. Enzymes have also been used to decrease swelling and, while some debate continues, there is increasing evidence that some benefit accrues. Allaben and co-workers¹ measured the volume of the hand and forearm of rhesus monkeys by water displacement. These appendages were then run through a hand-operated wringer and their volumes were subsequently followed post injury. They found edema was considerably less when the animals received enzymes (chymotrypsin in this study), and they noted the first day's dose was the most important. It was suggested that the enzymes should be continued for a total of four days.

There is no controversy on the foundations of treatment: cleansing, compressive dressings, elevation and appropriate surgery when needed. The injury is potentially disastrous and even with a paucity of initial findings treatment should be immediate and thorough.

Capt. Michael W. Davis, M.D.
98th General Hospital
APO New York 09034

^{*}See Minnesota Med 50:195, 1967.

References

1. Allaben, R. D., Posch, J. L., and Larsen, R. D.: An Experimental Evaluation of the Efficacy of Chymotrypsin in the Reduction of Edema in Crushed Extremities. *J Bone Joint Surg* 44-A:1:41, 1962.



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EDITORIALS



Owen H. Wangensteen, M. D.

May I through the columns of our distinguished Minnesota Medicine relay a message of appreciation and gratitude to my large Clinical Staff in the Twin Cities and to the physicians of Minnesota. In a very real sense, the Physicians of this wonderful community have contributed in a significant manner to the growth in stature and development here of a Great Medical Center.

As I leave the Department of Surgery to spend my remaining days and years in research and upon studies relating to the history of surgery, I would like to indicate to my competent staff and the physicians of Minnesota my warm appreciation of their loyal support of the Medical School, its Medical Center, and the Department of Surgery.

For me it has been a labor of love replete with happy associations and enduring satisfactions. For all this I shall always be eternally grateful to the good people of Minnesota.

Over future decades, the Medical School, I am certain, with continued support from the physicians of Minnesota will continue to grow in stature and in service to the people of this area, as it has over the first 80 years of its existence.

Owen H. Wangensteen, M.D.
Professor and Chairman
Department of Surgery

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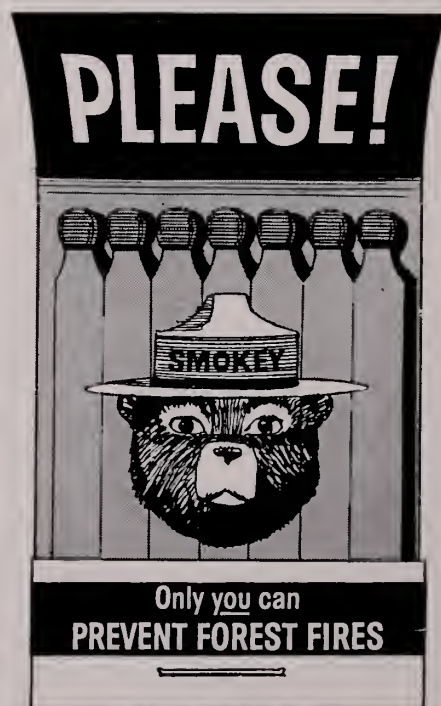
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"New" Intra-Articular Steroid

DR. PAUL BILKA's article in the April 1967* issue of MINNESOTA MEDICINE is worthy of comment on several counts. He reports on 298 intra-articular injections in rheumatoid arthritic patients using a new and commercially unavailable preparation called Triamcinolone Hexacetonide. It resembles the two most commonly used intra-articular steroids, namely Prednisolone tertiary Butylacetate and Hydrocortisone tertiary Butylacetate, in containing a TBA radical on C-21 plus an acetonide group on C-16 and C-17.

Dr. Bilka has clearly shown the superiority of the new Triamcinolone drug, with its immediate benefit equalling previously used drugs with a 90% plus benefit, but with its average duration of action being three months instead of one month with hydrocortisone TBA.

He also observed that in 35 joint injections a significant systemic effect from the steroid was noted. If this is true with this new most insoluble preparation, it is even more true with the currently available intra-articular steroids. The

physician should always assume the systemic effect could occur and act accordingly. A patient of mine with a very distant past history of peptic ulcer bleeding bled within 24 hours after receiving an intra-articular steroid. Also the physician should be conservative in his dosage. For example 50 mg. of hydrocortisone TBA is adequate for a knee joint and smaller doses for smaller joints. One should keep in mind that some preparations contain as much as 200 mg. of hydrocortisone equivalent per ml.

An interesting question is raised by Dr. Bilka. He comments on Hollander et al. reporting on Triamcinolone Hexacetonide as far back as 1961. The new Hollander text on arthritis mentions the same drug as the one of choice for intra-synovial therapy. Yet after six years of research use of the drug, it is not available commercially. Let us hope that Dr. Bilka's paper will prod the FDA and Lederle Laboratories into achieving its near future commercial release.

David A. Randall, M.D.
Minneapolis, Minnesota

*See Minnesota Med 50:483. 1967.

Of Machines and the Man

EPISTEMOLOGY, the formal philosophic inquiry addressing itself to the "How do we know issue?" always seems at the heart of scientific investigation. It operates at and across several levels, ranging from concepts of physiologic imprints on neural tissue (engram theory) to investigations into data accumulation.

This question frequently stifles biomedical investigation. We are dubious of facts offered to us based on an arithmetic mean of observation. The body of statistical lore has become so sophisticated that now we may (and sometimes rather pretentiously) say, "That is good data," or "This is bad data." We can be so introspective about the knowing and learning process that we sterilize productive thinking. And after all, results count for something if not almost everything in science: results in the strict sense of accumulation of data and its organization into a scale of relative approximations to the truth.

Now all this leads us to consider the development of the computer manipulation of physiologic measurements and programmed history forms. Asking a machine to do this is well within the scope of today's technology. One wonders though whether a machine can be programmed to tell us about and then suggest to us a solution to a patient's particular predicament as against a name and a treatment for his disease. What a machine most likely lacks today is what the poets call the tragic vision, the mutation of data into a fine human sensibility.

This aspect of the epistemologic inquiry is quite new. The translation of humanoid sensing into human tenderness and response may be possible soon. Till then the doctor will have to hold his patient's hand, perhaps with his other hand on the keyboard of an IBM.

Robert A. Maslansky, M.D.
Minneapolis, Minnesota



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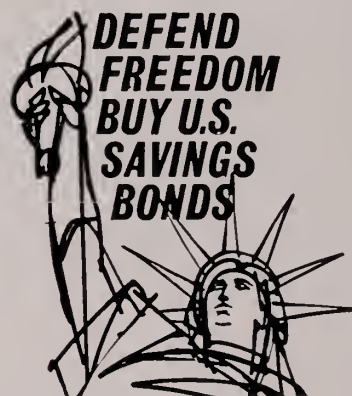
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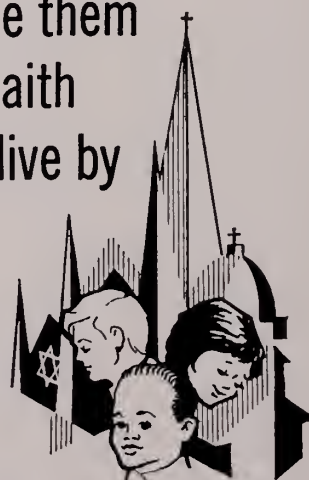
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RELIGION IN AMERICAN LIFE

Insects and Other Arthropods as Related to Human Health in Minnesota

IN MINNESOTA, insects and their relatives within the Phylum Arthropoda* are medically important to humans more as direct agents of discomfort or injury than as vectors of disease-producing organisms. This is primarily due to the fact that the State is situated in a northerly region characterized by extremes of temperatures.

Tularemia, or rabbit fever, a bacterial infection which occurs in Minnesota, may be passed by the bite of an infected tick or mechanically inoculated by the contaminated mouthparts of some bloodsucking insect. However, it is more often contracted by handling carcasses of infected rabbits. Meadow mice and other rodents may also harbor the organism. Plague, another bacterial disease maintained by various fleas in a vast rodent reservoir in the western half of the United States, has not been recorded in Minnesota but is found in adjoining western states. It is therefore possible that this organism may now exist undetected in Minnesota, constituting a potential hazard.

A rickettsial infection, Rocky Mountain spotted fever, occurs generally throughout the continental United States, with Minnesota no exception. The etiological agent is passed primarily in the saliva of a feeding infected tick; however, the number of recognized indigenous cases in the central states is relatively low. The last cases recorded in Minnesota were two in 1961.

Probably the most significant arthropod-borne infection of humans in Minnesota is Western encephalitis, produced by a virus carried by certain mosquitoes, presumably from a bird or other wild animal reservoir to humans and horses. This disease was of great importance around 1940 when a large number of cases occurred among humans and horses; but in recent years only a few infections have been noted. A second mosquito-borne arbovirus, that of St. Louis encephalitis, also occurs in Minnesota; but no human illness ascribed to this cause has been reported.

A large group of flies, typified by the house fly, *Musca domestica*, possesses a sponging type of mouthparts, making them incapable of piercing

and drawing blood. These flies may nonetheless become contaminated with any of a number of pathogenic microorganisms. This is especially true for flies that visit fecal materials or feed on exudates from wounds, eyes, or the like. They may either carry organisms externally from such a source or ingest organisms which then may be passed in a viable state via vomitus or feces.

The only insect-transmitted worm that might infect humans in Minnesota, aside from a remote possibility of a tapeworm infection, is the dog heartworm, *Dirofilaria immitis*. This worm is common in dogs and related hosts, especially in the Twin City area, and is presumably carried from host to host by mosquitoes. Although humans are fortunately not suitable for development of adult worms, there have been several instances recorded of apparently asymptomatic encapsulation of larval worms in human tissue. The broad fish tapeworm, *Dibothriocephalus latus*, also present in Minnesota, utilizes a crustacean early in its larval cycle, but the ultimate infection in man is from the fish, not the arthropod.

It is thus evident that the probability of contracting a pathogen from an arthropod is rather remote. Our primary concern, therefore, is with the direct effects insects may have on man. Minnesota is "blessed" with an over-abundance of bloodsucking flies, notably mosquitoes, black flies, horse flies, deer flies, punkies, and stable flies. With reference to mosquitoes, a noted entomologist, over 80 years ago, said, "The bravest man on the fleetest horse dares not cross some of the more rank and dark prairies of Northern Minnesota in June." This statement is as appropriate today as then and could well be expanded to include more than mosquitoes. When these bloodsucking flies feed, they inject a salivary secretion, and the reaction to this bite may vary from virtually none, to itching, to marked swelling around the site of the bite, and in some instances to a more extreme type of response which may require medical attention.

Certain ectoparasitic insects may need a more prolonged and intimate contact with man than the bloodsucking flies. Humans have two species

Continued

* See Test Your Word Score Page 1227.

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of lice—the human louse, *Pediculus humanus* (with body and head subspecies), and the crab louse, *Phthirus pubis*—restricted to man alone, living on or near the host and taking several blood meals a day. Bedbugs and fleas are not overly host-specific and will suck human blood if the opportunity presents itself.

The American dog tick or Eastern wood tick, *Dermacentor variabilis*, is extremely common in Minnesota, with the unfed overwintering female and male attaching to humans, as well as to other animals, in the spring and early summer. This tick is virtually the only tick in the State likely to be found attached to humans. Aside from the bite itself and possible secondary infection, this tick is responsible for producing tick paralysis in areas of the eastern United States, but apparently not in Minnesota.* The chicken mite (*Demanyssus gallinae*), the northern fowl mite (*Ornithonyssus sylviarum*), and the tropical rat mite (*Ornithonyssus bacoti*) may occasionally stray from their normal hosts and feed on man, producing a dermatitis. The North American chigger mite (*Trombicula alfreddugesi*) occurs at least in the southern half of Minnesota, and the bite of its parasitic larval stage results in an intense itching and the production of a reddish papule with a minute hemorrhagic center; the bites are found especially on areas where there is clothing pressure, such as under belts or socks.

In the United States there are very few species of spiders venomous to humans, but one of these is *Latrodectus mactans*, the black widow. This spider occurs in Minnesota, although it may be more prevalent in other parts of the United States. Occasional poisonings from the bite of the female may occur in Minnesota.

A number of hymenopterous insects, such as bees, wasps, hornets, yellow jackets, or velvet ants, may sting man by means of a specialized

ovipositor, and, by so doing, inject a venom. The reaction of man to these stings again varies widely, all the way from a transitory pain to rapid collapse and death. Although deaths are rare in proportion to the numbers stung, almost twice as many people die in the United States from bee and wasp stings as from snake bites.

Cases of myiasis—invasion of organs and tissues of man by fly larvae—are occasionally encountered in Minnesota. A skin maggot fly, *Wohlfahrtia vigil*, may deposit a clutch of larvae directly on the human skin, especially of very young children; these larvae will enter and excavate in the skin. Larvae of other assorted species of flies may be classed as occasional invaders of the intestinal tract or secondary invaders of wounds or natural cavities; but, as this is not their normal habit, the observation of viable fly maggots in a freshly passed stool may cause considerable alarm. Larvae of cattle warble flies, *Hypoderma* species, and horse bot flies, *Gasterophilus* species, while normally restricted to living within their livestock hosts, have been recorded from man. Since these flies exist in Minnesota, an occasional human infection may occur.

There are certainly other ways arthropods may affect humans. Some people who have become sensitized to insect particles may develop an allergic response; an asthmatic attack produced by inhalation of air-borne setae** and scales of moths is illustrative of this. Accidental injury may occur to sense organs following collision with or entry by any of a number of insects.

There are a few people who suffer from hallucinations and develop extreme anxieties regarding imagined insect or arthropod attack. These people, suffering from what is termed "entomophobia" or "delusory parasitosis," present a real challenge to those attempting diagnosis and treatment.

Roger D. Price, Ph.D.†
St. Paul, Minnesota

Theodore A. Olson, Ph.D.‡
Minneapolis, Minnesota

* See Minnesota Med 50:383, 1967.

** See Test Your Word Score Page 1227.

† Department of Entomology, Fisheries, and Wildlife, University of Minnesota, St. Paul.

‡ School of Public Health, University of Minnesota, Minneapolis.

Kiss

Kiss: the anatomical juxtaposition of two orbicularis oris muscles in a state of contraction.

—Henry Gibbons

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O. Erik Hallberg, M.D.
Rochester, Minnesota

*Saunders, W. H.: Epistaxis. Minnesota Med 50:849, 1967.

Test Your Word Score

Syllabub—*a dish made by mixing wine with milk, forming a soft curd (page 1180).*

Grandiosity—*noun, from grandiose: imposing, bombastic (page 1189).*

Sessile—*attached by a broad base (page 1201).*

Vector—*carrier (page 1203).*

Clubbing—*proliferative change in soft tissue of terminal phalanges (page 1208).*

Phlegmasia alba dolens—*phlebitis of the femoral vein (page 1215).*

Arthropoda—*comprising articulated animals: spiders, crustaceans and so forth (page 1223).*

Setae—*bristles or hairs (page 1225).*

Etymologic—*adjective, from etymology: word derivation (page 1229).*

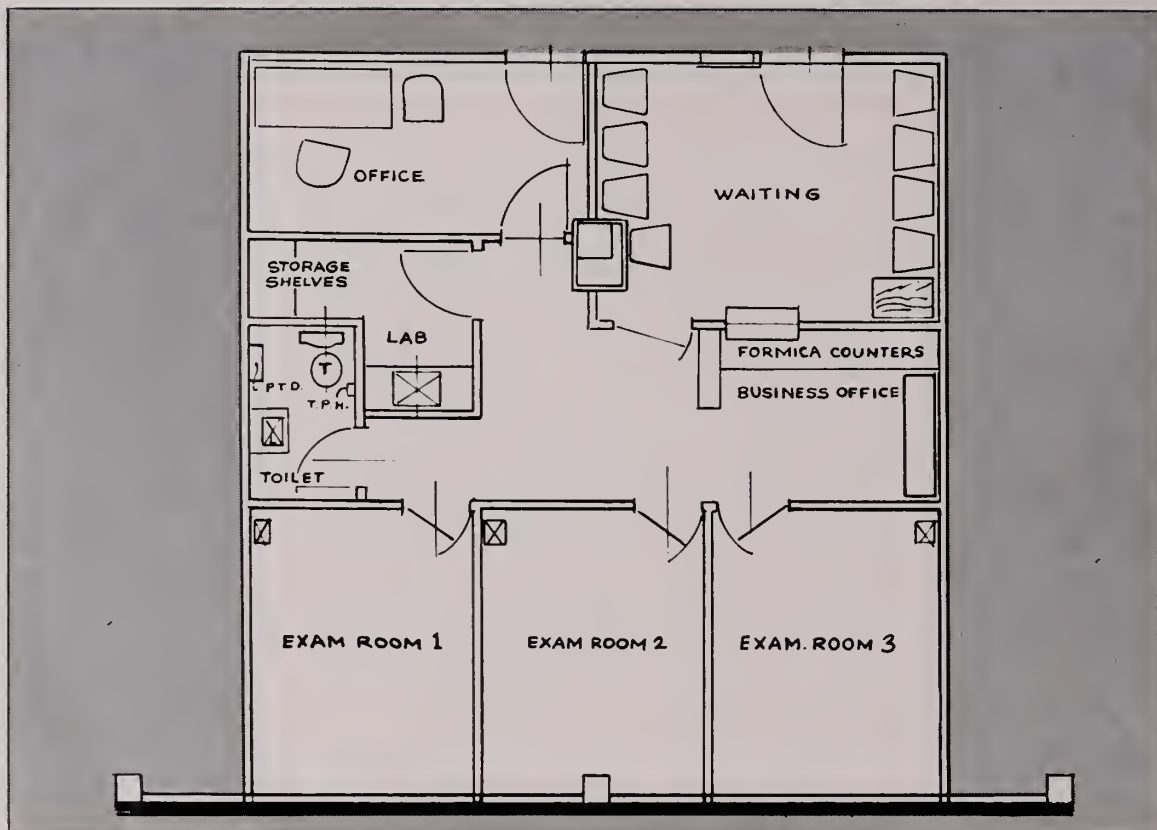
Cor triatriatum—*a heart with three atrical chambers, the left atrium being subdivided by a transverse septum with a single small opening which separates the openings of the pulmonary veins from the mitral valve (page 1243).*

Cytogeneticist—*a geneticist who specializes in the study of chromosome and gene behavior (page 1258).*

Animals, we have been told, are taught by their organs. Yes, I would add, and so are men, but men have this further advantage that they can also teach their organs in return.—Goethe

In a room where a man was dying, a nurse, young, and a bit scared, turned to a minister and said, "If he dies, I don't know what I'll say to his wife." The minister said, "Don't say anything. Make her a cup of tea."

Leslie Weatherhead



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You May Be Right

In the May, 1967 issue of MINNESOTA MEDICINE (p. 673) there appears an editorial which I was invited to write, in a historical, nostalgic manner, referring in particular to the physicians who had practiced medicine in Minnesota for the major part of the past fifty years. I was given the names of twelve men to be inducted into the Fifty Year Club at the annual meeting, and I mentioned them in my article. Because of the proximity of the deadline, I did not have an opportunity to check the galley proofs, so I did not see the finished article until the May issue reached me.

In general, your editors were very kind to me, but there are a few errors which I must correct.

First, after carefully counting on my fingers and verifying with my abacus, I find the names, photographs and biographic sketches of thirteen, not twelve physicians. I mention this because you and others may be checking my arithmetic. Upon inquiry I learned that the name of Dr. A. E. Venables had inadvertently been left out of the list which had been handed me.

Secondly, I described the influenza outbreak of 1917 as more vicious and destructive than any epidemic of modern times. One of your editors substituted the word "insidious" for "vicious." It was not at all insidious. We had ample warning that it was coming but we could do nothing to prevent it.

Thirdly, on page 677, the paragraph at the right, above, should read, "Of the twelve physicians whom we honor this year, there are some whom, alas, I know very slightly or not at all, but about whom I have heard glowing reports, both personally and professionally."

Finally, on page 675, right, above, I had written, "if some of us interns were a little awkward and lacked *panache* the girls didn't seem to mind." The word "panache," as you know, means literally a plume or bunch of feathers, as an ornament on a helmet. It also implies dash or verve, like a knight on a white charger. In contemporary usage, a near-miss as a synonym would be "glamour," but they are not identical in meaning. Really, it should not be necessary for me to have to insert the term "(sic)" after every word at which I fear for my etymologic* life.

Well, somewhere along your editorial line someone extracted "panache" and inserted "skill." Sir, in behalf of my classmates and myself, I object strenuously to your revelation of our amatory inadequacies at that tender age, however justified these charges may be. Darn it!

Virgil J. Schwartz, M.D.
Minneapolis, Minnesota

EDITOR'S NOTE: — *Decked out with an "abacus" and a "panache," I am sure that any man, in this non-Grecian-French romantic era, could cut a great figure and would need no "etymologic" explanation to convince the object of his amour of his good intentions. We apologize for the deletions.*—C.O.R.

*See Test Your Word Score Page 1227.

Examination

You must look into people as well as at them.—Lord Chesterfield

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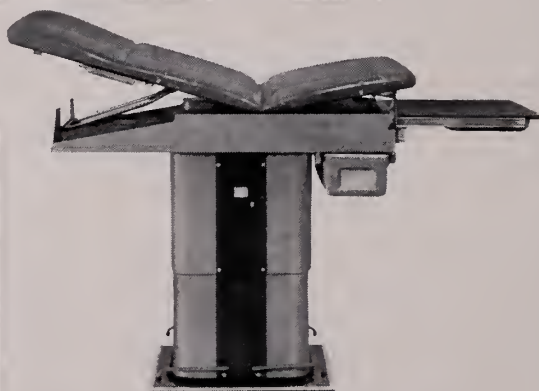
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The Editor's Soliloquy

Professional Common Sense

If it seems right, there is a strong probability that it is; if it doesn't seem right, there is an equally strong probability that it isn't. To so conclude without a plethora of substantiating evidence is what might be called common sense—a term that might well be considered a misnomer, since common sense belies its name by being rather rare.

It is difficult to pinpoint the qualities that go to make up an individual who seems to possess this uncommon quality; but all of us are aware of having known such persons. They have the ability to sift facts from opinion, distinguish the pertinent from the irrelevant, the major from the minor; they are immune to delusion and wishful thinking as well as to unwarranted projection and extrapolation.

In the practice of medicine some physicians seem to require an overabundance of laboratory data, whereas others demand none. In the midspectrum between these two approaches is the physician whose excellent clinical judgment impels him to make only those few additional studies required to substantiate his tentative diagnosis, but whose humanistic attitude, on the other hand, impels him to consider a host of other items, clinically extraneous but most significant in the elusive correlation between the patient per se and his disease. With imagination and insight such a doctor takes into account such basically unrelated items as patient apprehensions, responsibilities, employment, expenses, and the little worries that afflict most everyone—the total framework wherein the patient must be evaluated.

Whether the doctor resolves his patient's personal problems or not, at least by sharing them he lightens them for the patient and his family—a creditable achievement in any context. Such a doctor is more interested in prognosis than in diagnosis, more concerned with probable morbidity than with a remotely possible mortality, more occupied with the emotional adjustment of the patient than with the etiology of his disease, and more cognizant of his patient's physical welfare than he is of the tedious details of the hospital record.

This is what might be called professional common sense.

Carl O. Rice, M.D.

Old Doc Hess Says: After two or three husbands a woman can, if cautious, accumulate a fairly sizable bank account.—COR

Non-Sequitur

Drink wine and you will sleep well. Sleep and you will not sin. Avoid sin and you will be saved. Ergo, drink wine and be saved.—German saying.

Exercise

Whenever I feel like exercise, I lie down until the feeling passes.

—Robert Hutchins

Life-saving words. Required by Congress to appear on all packages of cigarettes.

Unquestionably an important step forward in the dramatic battle to decrease the mortality and morbidity from cigarette smoking.

But in the nation's efforts to reduce death and disease related to cigarette smoking, the most significant influence—the key figure—is you, doctor. The advice of the physician in matters of health is more authoritative and persuasive than that of anyone else.

In the area of cigarettes and health, the importance of the physician's attitude and his *personal action* cannot be overemphasized. That he has indeed taken personal action is indicated by the impressive statistic showing that only 30% of the doctors in America are cigarette smokers today!

The American Cancer Society's concerted educational campaign on the hazards of cigarette smoking—plus government regulations—will be major factors in guiding each person's approach to this problem.

But in the final analysis, doctor, it is *your* words that your patients will heed. It is you who have the best chance of actually helping an individual to stop smoking or to prevent him from starting.

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The Viewing Box

Dyspnea in a Fifty-Three-Year-Old Female

THIS 53-YEAR-OLD white female was seen in the emergency room on February 21, 1967. Her chief complaint was dyspnea of one day's duration. In addition she stated that she had had "a cold and hoarseness" for about one month. She had no sputum production and a normal temperature. Her blood pressure was 170/70. On physical examination the patient appeared to be older than her stated age; the examination was otherwise normal.

This patient has been treated for ten years for hypertension and urinary tract infections. In 1961, a unilateral nephrectomy was performed for a calcified cyst. Blood chemistries done in October 1966 included a uric acid of 8.6 mg. %, BUN of 74 mg. % and creatinine of 8.2 mg. %. The diagnosis is now chronic pyelitis and pyelonephritis with end-stage kidney disease.

Radiographic examination (Figure) demonstrated a normal sized heart with the hilar and peripheral changes of pulmonary edema. Also noted were Kerley's "B" lines which are indicative of chronic lymphatic congestion. No frank pleural effusions were present.



Figure

What is your diagnosis? (See next page.)

Diagnosis: Pulmonary edema secondary to chronic renal failure.

Discussion

With the finding of a normal-sized heart with a pulmonary hilar "butterfly" picture, with or without pleural effusion or Kerley's "B" lines, a differential diagnosis would include:

1. Over-hydration via fluids and blood.
2. Drowning.
3. Inhalants—toxic agents, hydrocarbons, etc., and oral ingestants—kerosene.
4. Elevated BUN (chronic renal failure).
5. Acute myocardial infarct with failure.
6. Pericarditis.
7. Periarteritis.
8. Carcinoid.
9. Pheochromocytoma.

It was felt that this radiographic picture was due to chronic renal disease rather than hypertensive cardiac disease, since the severity of the renal disease had increased, as supported by the laboratory studies. In addition the blood pressure remained only slightly elevated, and the heart size remained within normal limits.

John McManus, M.D.
John Holder, M.D.
St. Paul-Ramsey Hospital
St. Paul, Minnesota

References

1. Gibson, D. S.: Haemodynamic Factors in the Development of Acute Pulmonary Edema in Renal Failure. *Lancet* 2:1217, 1966.
2. Heitzman, R. E., and Ziteu, F. E.: Acute Interstitial Pulmonary Edema. *Amer J Roentgen* 95:2:291.
3. Rigler, L. G., and Surprenant, E. L.: Pulmonary Edema. *Seminars in Roentgenology* 2:1:33.
4. Simon, Morris: The Pulmonary Vessels, Their Hemodynamic Evaluation Using Routine Radiographs #2, pp. 363.

Ancient Arabs in Medicine

RHAZES (865-925) was perhaps one of the first men to use sutures of animal gut for the repair of abdominal wounds.*

AVICENNA (980-1037) attended the sick without fees, and says he was rewarded by discovering new methods of treatment.*

AVENZOAR (12th Century A.D.) is interesting as probably being the first to suggest nutrition per rectum.*

AVERROES (12th Century A.D.) wrote much on the healing art, but his observation that smallpox does not attack the same person twice constitutes his sole original contribution to medicine.*

* Massengill, S.E.: *A Sketch of Medicine and Pharmacy*, The S.E. Massengill Co., Bristol, Tenn.-Va.

Medical Seminar

Irradiation and the Fetus

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THE PROBLEM OF irradiation and the fetus not only involves the effects of radiation on the fetus but also includes the complexities of population genetics. Man is exposed to many sources of radiation (Table 1), and from each source he receives a certain estimated dose of radiation. Natural or background radiation, which varies with locality, is estimated to provide 100 to 150 milliroentgens per year to the gonads.^{1,2} Thus the gonadal dose of radiation received from background radiation by the average individual by age 30 years is in the range of 3.0 to 4.5 roentgens. Among the sources of artificial radiation to which man is exposed, by far the most significant is the medical use of x-rays, which has been estimated to contribute a gonadal dose of 3.0 r. to the average person by the time he is 30 years old. Thus, the amount of irradiation received by the population in general from the medical use of x-rays is about equal to that received from all sources of natural radiation. The estimated 30-year gonadal dose received from radioactive fallout from nuclear weapons testing is about 0.5 r.

Radiology has been employed in obstetrics for a number of clinical situations: (1) investigation of possible cephalopelvic disproportion, either antepartum or intrapartum; (2) determination of fetal maturity; (3) determination of fetal position, when clinical findings are inconclusive or suggestive of an abnormal position; (4) determination of placental localization, when there is bleeding during late pregnancy or prior to amniocentesis; (5) investigation of excessive uterine enlargement, and (6) investigation of suspected fetal anomaly or confirmation of fetal death. In addition to these obstetric indications, roentgenography may be indicated for the inves-

tigation or work-up of any medical condition occurring coincidentally during pregnancy.

Diagnostic Procedures During Pregnancy

Common Diagnostic Procedure

In any consideration of the radiation doses involved in various diagnostic procedures, there is one fundamental concept, namely, that radiation exposure during pregnancy always involves both genetic and somatic effects by virtue of simultaneous exposure of both maternal and fetal gonads; partial somatic maternal exposure; and partial- or total-body irradiation of the fetus.

In regard to the diagnostic x-ray studies most commonly performed during pregnancy, exclusive of pelvimetry or placental localization, investigators have reported various doses to maternal

TABLE I
Sources of Radiation to Man

Natural radiation (background radiation)
External sources include cosmic radiation and radiation from naturally occurring radioactive substances (uranium, thorium, actinium, and so forth)
Internal sources include naturally occurring radioactive elements which are deposited or incorporated in the body (⁴⁰ K, ¹⁴ C, ²²⁶ Ra, and so forth)
Artificial radiation
Radioactive waste from atomic industry
Radioactive fallout from nuclear explosions and testing
Occupational exposure of certain workers such as physicians, particularly radiologists, dentists, atomic energy workers, users of radioactive isotopes
Medical use of x-rays for detection, diagnosis, and treatment of disease
Miscellaneous group of radiation emitters, such as TV receivers, watches with luminous dials, x-ray units for shoe fitting

Continued

and fetal gonads (Table 2). The considerable variation between some of these doses for the same examination depends primarily on the particular x-ray technique and routine used by each investigator. The explanation for the difference between the data of Osborn and Smith⁷ for dosage to fetal gonads in comparison to those dosages measured by the other investigators to maternal gonads for the same examination is due to the formers' assumption that if the fetal gonads were exposed only to scatter radiation, the dose would be the same as that to the maternal ovaries. If, however, the fetal gonads are exposed directly to the central beam of x-rays, the dose received would be the geometric mean between the dose to the maternal ovaries and the dose to the maternal skin.⁷ Notably, more than 80% of the genetically significant gonadal irradiation that results from roentgenography is produced by radiation secondary to the five examinations listed in Table 2, plus pelvimetry.

Radiation Secondary to Pelvimetry

With respect to radiation secondary to pelvimetry, numerous studies have been made to assess the amount of irradiation to maternal and fetal gonads. Despite the various techniques used to calculate gonadal doses, such as implanting ionization chambers in phantoms or cadavers or measuring the dose delivered to the posterior vaginal fornix, considerable variation in the dosages obtained has resulted (Table 3). Some authors^{4,11} have simply stated that the maternal gonadal dose from pelvimetry varies from 2 to 4 r., whereas the fetal gonadal dose ranges from 0.50 to 7.0 r.

There are certain other generalities regarding pelvimetry with which most investigators are in complete agreement. First, the use of high-kilovoltage techniques, high-speed intensifying screens, high-speed films, better filtration, and shielding can substantially reduce gonadal doses.

TABLE 2
Gonadal Dose from Diagnostic X-Ray Procedures (in Milliroentgens)

Procedure	Maternal Gonad				Fetal Gonad
	Stanford and Vance ³	Ardran and Crooks ¹	Cooper and Williams ⁵	Martin ⁶	Osborn and Smith ⁷
Chest	0.07	0.02	0.06	0.07	0.07
Lumbar spinal column	669	350	780	1,025	1,540
Intravenous pyelogram	1,290	570	468	1,360	3,210
Abdomen	200	75	234	203	580
Pelvis	210	80	245	800	800

TABLE 3
Gonadal Dose from Pelvimetry (in Roentgens)

Site	View	Bewley and Associates ⁸	Berman and Sonnenblick ¹	Ritter and Associates ¹⁰	Lebherz and Ellinger ²
Maternal gonad	Inlet	0.5	0.4	0.4	—
	Outlet	0.03	0.4	0.4	2-4
	Lateral	0.10	1.2	3.5	—
Fetal gonad	Inlet	2.8-4.6	—	0.9	—
	Outlet	0.01-0.02	—	0.4	3-5
	Lateral	0.06-0.14	—	1.3	—
Fetal total body		1.2	—	—	1-3

Second, the inlet view of the pelvis, which is generally taken in the Thoms position, contributes about two thirds of the total dose of radiation from a standard, three-film pelvimetry series.⁸

Davis and Hunt¹² described the rationale behind the two-film pelvimetry technique used at the Mayo Clinic, in which one view is an inlet view of the pelvis taken in the Thoms position and the other a lateral view of the pelvis taken in the standing position. Only if a midplane contraction is found on both films is an outlet or subpubic arch view taken. Thus, by performing the outlet view only as an additional study when clinically indicated, they estimate that the total dose of irradiation received is reduced about 30% from that obtained with a three-film technique.

Radiation Secondary to Placental Localization

Ever since Browne¹³ reported the use of radioactive sodium for the first isotope placental localization in 1951, extensive work has been done in this field in an effort to decrease irradiation, provide greater accuracy, and find the ideal tracer substance for this examination. The basic requirements for a suitable radioactive material for placentography include a sufficiently long half-life to facilitate its storage, a short enough half-life to decrease radiation dosage, and reduced beta-particle emission to further decrease tissue irradiation. In addition, the tracer should be retained in the vascular compartment long enough for completion of the test but excreted rapidly thereafter to minimize radiation.

The characteristics of the most commonly used isotopes for placentography are summarized in Table 4.

The amounts of maternal gonadal, fetal gonadal, and fetal thyroid irradiation received from isotope placentography have been described by various investigators and have been compared with doses received from conventional, soft-tissue, x-ray placentography (Table 5).

Effects of Radiation on Embryogenesis

The earliest animal work in the field of experimental irradiation was concerned chiefly with the production of abnormalities. Job and co-workers,¹⁷ in 1935, while studying the effects of irradiating rats at different times during gestation, produced specific abnormalities or deformities, depending on the gestational age at the time of irradiation. They thereby advanced the concept of "critical periods" in the development of the embryo as a whole or for certain of its organs or systems, during which time irradiation would produce specific defects. In 1950 Russell¹⁸ demonstrated that these critical or susceptible periods of development for a given organ or organ system could be lengthened by increasing the dose of x-rays administered. Brent,¹⁹ in 1960, proved that it was the direct irradiation of the fetus which induced teratogenesis rather than placental injury or maternal metabolic dysfunction that affected the fetus secondarily. Otis,²⁰ in 1949, plotted more than 80 cross-reference points between the embryonic development of the human and mouse and obtained a remarkably smooth curve, thus indicating the theoretic possibility of predicting the critical period for production of abnormalities in man. All abnormalities studied in the human had critical periods that occurred between the second and the sixth postconceptional week—at the time of major organogenesis²¹ (Figure).

TABLE 4
Characteristics of Commonly Used Isotopes
for Placentography

Isotope	Half-life	Emissions, Avg. Mev.	
		Beta	Gamma
Iodine-131	8 days	0.2	0.4
Iodine-132	2.3 hours	0.5	0.8
Technetium-99	6 hours	—	0.14

TABLE 5
Radiation Dose in Placentography

Site	Source, Milliroentgens				
	X-ray ³	¹³¹ I ¹⁴	¹³¹ I ¹⁵	¹³² I ¹⁴	⁹⁹ Tc ¹⁶
Maternal gonad	1,000	15	12	10	9.4
Fetal gonad	1,000	7	5	5	2.6
Fetal gonad	1,000	4,900	2,500	130	20
Fetal total body	1,000	—	6.5	8	14

Continued

The most radiosensitive stage in the life history of a cell is during its transformation from the embryonic to the adult stage. During the embryonic period, 18 to 38 days after conception, such transformations are occurring in nearly every one of the tissue varieties in the human embryo.²² Thus, it was presumed that irradiation, at a time of rapid growth rate, DNA replication, cell division, and differentiation, caused the variety of effects seen during the early post-conceptional period.

Other investigators^{23,24} working with mice discovered that irradiation after fertilization, but prior to implantation, was followed by an "all or none" response to the radiation. Results of these studies showed a high incidence of prenatal death, in many series as high as 80%,²³ whereas the surviving embryos were apparently normal²¹ (Figure). However, irradiation after completion of organogenesis resulted in minimal prenatal mortality and marked reduction in detectable malformations²¹ (Figure).

Finally, the likelihood of producing neonatal malformations in the human probably is minimal if the dose of irradiation is less than 10 to 20 r. Currently, there is no experimental or clinical evidence that radiation dosages of the order involved in routine diagnostic x-ray studies, exclusive of certain high-dose fluoroscopic procedures, will produce neonatal malformations in the hu-

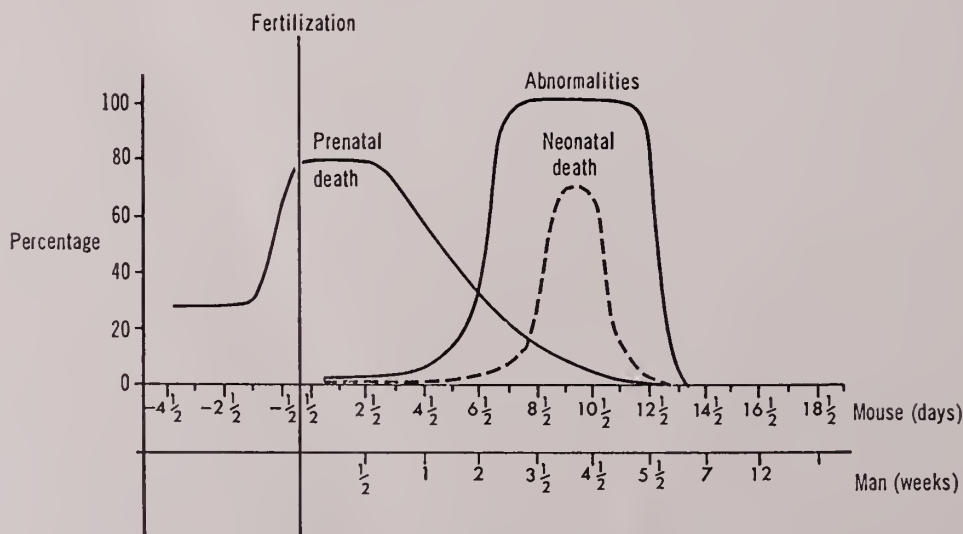
man.

Irradiation During Pregnancy

The best studies of radiation therapy during pregnancy are those reported by Murphy,^{25,26} Goldstein and Murphy,²⁷ and Jones and Neill.²⁸ Murphy,²⁶ in 1929, reported the outcome of 625 pregnancies in which the mother was exposed to pelvic radium or roentgen therapy either before or after conception. His study showed that irradiation before conception resulted in 0.9% stillbirths, 3.2% fetal deaths and 1.7% deformities, whereas irradiation after conception resulted in 0.0% stillbirths, 6.7% fetal deaths, and 33.7% deformities.

Goldstein and Murphy²⁷ reported a series of 75 infants born to mothers who had received therapeutic doses of pelvic radium or roentgen therapy during pregnancy for conditions such as uterine myomas, metrorrhagia, and pelvic neoplasms. Of the 30 infants (40%) who were affected by the irradiation, 70% had abnormalities of the central nervous system, the most common of which was microcephaly. Furthermore, 24 of the infants (80%) who sustained irradiation injuries had been exposed during the first trimester.

Jones and Neill,²⁸ in 1944, presented statistics from radium treatment of carcinoma of the cervix during pregnancy. Their results closely cor-



Figure

Incidences of prenatal and neonatal deaths and of abnormalities at term after irradiation of mice at various intervals. The corresponding estimated chronology for man is shown. (Reproduced with permission from Brill, A. B., and Forgetson, E. H.: *Radiation and Congenital Malformations*. Amer J Obstet Gynec 90:1149, 1964.)

roborated Strauss²⁹ earlier work in that both studies revealed the risk of microcephaly to be about 20% after therapeutic pelvic irradiation during pregnancy.

The effects of the atomic bomb explosions on pregnant females offer further confirmatory data to the previously mentioned animal and human studies. Of the 205 women who were in the first trimester of pregnancy at the time of the Hiroshima explosion, 33 delivered microcephalic infants. As would be expected, the majority of these patients were in the early part of the first trimester of pregnancy when exposed. Also, in most of the instances, the mother was located 1.5 to 2.0 km. from the hypocenter of the explosion, where the average radiation was estimated to be about 100 rads.³⁰

More recently, epidemiologic studies have provided further information regarding the long-range effects of irradiation on the fetus. Although there still is conflicting evidence in the literature, it appears that both high- and low-level doses of radiation may be capable of producing malignancy or leukemia, presumably because of chromosomal abnormalities induced by the radiation. Evidence supporting the influence of high-dose radiation in the production of malignancy or leukemia is obtained from the Atomic Bomb Casualty Commission's report of increased incidence of leukemia among the survivors of Hiroshima and Nagasaki,³¹ as well as from the increased incidence of thyroid cancer noted after irradiation of the thymus in infants so treated for thymic enlargement.³²

What are the effects of low-dose radiation, specifically those from diagnostic x-rays, and what is the etiologic relationship of such radiation to malignancy or leukemia? Stewart and associates,³³ in 1956, in a large retrospective study done in England, found what they believed was a definite causal relationship between prenatal abdominal x-ray examinations and the subsequent development of malignant disease in the children born of these pregnancies. In 1958 Stewart and co-workers³⁴ published an expanded series in which they reversed their original opinion and concluded that diagnostic irradiation did not account for the recent increase in childhood malignancy. Court Brown and associates,³⁵ in 1960, collected follow-up data on nearly 40,000 children whose mothers had received diagnostic radiation to the abdomen or pelvis during preg-

nancy and found no causal relationship to the incidence of leukemia. In 1962 MacMahon³⁶ published the most extensive report in this field. Working with a control population of nearly 750,000 children, he found that: (1) the incidence of prenatal x-ray exposure in the control group was 10.6%; (2) the incidence of prenatal x-ray exposure in children who died from cancer or leukemia was 15.3%, and (3) the mortality from leukemia was 40% higher in those irradiated in utero than in the nonirradiated control group.

At present the evidence seems to favor the hypothesis that low doses of radiation from diagnostic x-ray examinations may be leukemogenic to the developing fetus.

Genetic Effects of Radiation

The tremendous amount of work that has been done on the genetic effects of radiation since Muller³⁷ first reported the mutagenic action of radiant energy in 1927 has led to the development of certain basic precepts in radiation genetics.

1. There is no threshold dose of radiation required to produce genetic mutations. Rather, the genetic damage produced by radiation is cumulative over the years. This concept is referred to as the linearity response.

2. The effect of radiation is to increase the number of spontaneously occurring mutations rather than to produce new types of mutations.

3. Genetic mutations are almost always undesirable in that they produce deviations from normal which then continue to be duplicated and passed to succeeding generations.

4. Genetic mutations may be recessive, intermediate, or dominant, but regardless of what they are, they generally result in decreased longevity, increased susceptibility to disease, and decreased fertility.

5. Only a fractional portion of induced genetic effects will be manifest in the first post-radiation generation. With each successive generation, more expression of the genetic effect will be apparent.

6. The doubling dose concept is the amount of radiation necessary to produce the same number of mutations which occur spontaneously in a given time. For man, the doubling dose has been estimated to be in the range of 30 to 80 r., probably about 50 r.

Continued

7. Further knowledge in the area of radiation genetics is being derived primarily through the use of cytogenetic techniques.

Medicolegal Aspects of Prenatal Irradiation

Recent developments in legal precedence make it mandatory for all practicing physicians to exercise maximal prudence in their use of radiation. Currently the law is tending to acknowledge the legal existence of the fetus or embryo from the time of conception onward, on the grounds that the conceptus has an independent existence except for sustenance and protection provided by the mother. The law already protects the unborn child's property rights and grants it protection under criminal law.³⁸ The basic legal problem involved in prenatal irradiation is the establishment of a causal relationship between the radiation exposure in question and the alleged effect thereby produced.

More recently, recovery of damages has been allowed for mental distress on the part of an exposed expectant mother because of her fear of having a defective child after irradiation, despite the fact that her infant was normal at birth.³⁸ Thus, by precedence, the physician may be held liable for the expectant mother's mental anguish over the fear for the intactness of a conceived but as yet unborn child.

Some standards and recommendations have been proposed relative to radiation protection of the population in general and more specifically in the management of the obstetric patient. The Genetics Committee of the National Academy of Science recommended that for the general population the average gonadal exposure should not exceed 10 r. prior to age 30, whereas for a given individual the accumulated gonadal exposure dose should not exceed 50 r. by the time a person reaches the age of 30 years.¹ Neither of these recommendations, nor those expressed by the

International Commission on Radiological Protection,³⁹ provides for the inclusion of the amount of radiation contributed by the use of x-rays for medical diagnostic or therapeutic purposes. Instead, no specific controls or limits were established in this area intentionally, as it was believed that this represented a medical determination, and hence is best left to the prudent, informed judgment of the individual physician.

With specific reference to the use of diagnostic x-rays in women of childbearing age, most sources concur with the recommendations of the International Commission on Radiological Protection.³⁹ During the period of maximal radiosensitivity of the embryo, which is between the second and the sixth week after conception, most women are not aware of the possibility of their being pregnant. Therefore, it was recommended that, whenever possible, x-ray examinations of the abdomen or pelvic areas in women of childbearing age should be performed only during the first 10 days after a regular menstrual period that is of normal intensity and duration. As with so many other decisions in medicine, the physician must balance the probability of the benefits derived by his actions against the possibility of harmful effects to the patient.

Summary

The pregnant female is exposed to both natural and artificial sources of radiation. Important sources of artificial radiation to the obstetric patient are diagnostic x-ray procedures such as those of the chest, spinal column, kidney, abdomen, and pelvis; radiation secondary to pelvimetry; and radiation secondary to placental localization. Radiation does affect embryogenesis and has been associated with various fetal malformations. Irradiation during pregnancy must be carefully considered both from the clinical and the medicolegal viewpoint, prior to its utilization.

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Rochester: Resident in Obstetrics and Gynecology.

References

1. National Academy of Sciences: The Biological Effects of Atomic Radiation: A Report to the People. From a Study. National Academy of Sciences — National Research Council, Washington, D.C., 40 pp., 1956.
2. Leberherz, T. B., and Ellinger, F.: Radiation and Pregnancy. *Med Ann DC* 31:67, 1962.
- 3-39. May be secured from the author or the reprints.

The more intelligent a man is, the more originality he discovers in men. Ordinary people see no difference between men.—Pascal

Clinical Path Conference

Cyanosis, Polycythemia, and Sudden Death in A 42-year-old Man

A 42-YEAR-OLD married laborer entered St. Barnabas Hospital on January 13, 1967. He complained that he was short of breath and that his legs were swollen. Although his respiratory difficulties grew worse just before he was hospitalized, he said he had had "trouble breathing" since he was ten years old. This, however, had not incapacitated him. He had served two years in the Navy, sired four children, worked on a loading dock for a wholesale firm, held down other jobs requiring physical effort, and continued to smoke three packs of cigarettes a day.

When questioned further, he said his ankle edema had slowly increased during the previous three months. But what really bothered him, he added, was an urge to sleep. His sleeping habits caused problems at work and at home. Frequently he fell asleep while in the bathroom and would awaken only when roused by his wife or another member of the family.

He was first aware of difficulty breathing when a ten-year-old youth in California. When he was thirteen, he saw a doctor because of an episode of rapid heart beat. Later, in his 20's, another doctor informed him he had an arrhythmia, digitalized him and, when the patient had bouts of tachycardia, placed him on quinidine. Despite this history, he passed the physical examination for the Navy and served two years. According to the patient, Navy physicians never told him that he had any specific disease or that he had a heart murmur.

The patient first came to St. Barnabas in 1964 while on vacation from California. He was seen in the outpatient department because of a fast heart rate, and an electrocardiogram showed paroxysmal tachycardia with right bundle branch block. He was given six grains of quinidine every two hours and converted to a regular rhythm. Then he was maintained on digitalis for two years before he discontinued the drug of his own accord.

Despite his health problems, he worked steadily. He lifted 100-pound bales of twine during the day and drove a snow plow at night. He continued both jobs until a week before he was admitted. Then ankle edema, fatigue, dyspnea on exertion, and finally shortness of breath while sitting or lying in bed forced him to come to the hospital.

Physical Examination

He was a mildly cyanotic muscular male who breathed heavily and complained of headache. His pulse was 105, respirations 48, temperature 100, blood pressure 130/70, and weight 238 pounds. Crepitant rales were detected at both lung bases. Different examiners could hear no heart murmurs. The fingers showed no clubbing. The liver and spleen were not palpable. The lower legs, which were swollen and showed a taut glistening skin, pitted when pressed. The physician

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who admitted the patient diagnosed congestive heart failure and, because the patient was a big man with a history of somnolence, also suggested Pickwickian syndrome.

Laboratory Data and Course

A circulation time done the day he was admitted was 24 seconds. He was then rapidly digitalized and put on a low-sodium diet. The first blood work included a hemoglobin of 18 grams percent, a hematocrit of 63 percent, a wbc. of 10,400 with 80 polymorphonuclear leucocytes and 10 band forms, and a platelet count of 255,000. The blood urea nitrogen was 11 mg./100 ml., the cholesterol 195 mg./100 ml., and the serum electrolytes normal.

During his first three hospital days, he quickly lost 20 pounds and his edema subsided. Because of his polycythemia, 500 ml. of blood was removed from his arm. Although his headache abated, he remained cyanotic and his heart continued to fail.

On January 17, four days after admission, he became apneic. He was resuscitated, but his breathing was shallow and rapid. A pH. was 7.46, and the carbon dioxide content was 37 mcq/l. An anesthesiologist tried to improve his respiratory exchange by giving oxygen under 25 mm. of water pressure. When the patient failed to improve, the anesthesiologist increased the pressure to 40 mm. of water. Again the patient stopped breathing. This time he did not respond to resuscitative measures.

Discussion

Dr. Donald Bohn:*

Before I discuss this patient's story, could I see the x-rays?

Dr. Philip Olson:**

Films of the chest taken on January 13 and 17 show prominent vessels in both lung fields. His diaphragms are high, and he obviously has no emphysema. I see no edema or congestion. The heart is transverse. His left heart does not appear hypertrophied, but his right heart border extends more to the right than usual. I don't have a lateral film to see whether his right ventricle bulges, but his right heart looks big.

The proximal two thirds of the lung vessels are dilated but then disappear peripherally. When I see a film like this, I think first of an acute coronary with slight heart enlargement but without pulmonary edema. I cannot make out septal lines, but I note some basilar atelectasis, presumably due to high diaphragms and lack of excursion. With this patient's history of pulmonary resistance, I would consider pulmonary fibrosis, pulmonary hypertension (primary or secondary), and right heart hypertrophy with failure.

Electrocardiograms

This patient had two electrocardiograms while he was in the hospital. The admitting cardiogram showed right axis deviation and nonspecific ST wave changes. Four days later, the day he died, the pattern changed profoundly. Though he had received digitalis, the right axis deviated more to the right, and

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**Radiologist, St. Barnabas Hospital.

the cardiogram disclosed more right ventricular strain. Neither of the tracings shows arrhythmias.

Differential Diagnosis

This man presented with heart failure, a prolonged circulation time, massive edema, and polycythemia with a hematocrit of 63 percent. He slept often, sometimes at embarrassing moments. He had no cough or murmurs, yet he deteriorated rapidly, stopped breathing, was resuscitated with the help of positive pressure breathing, and then died.

Immediate Cause of Death

First, let me dispense with the immediate cause of death. I think he had a pneumothorax. The oxygen had to be given at extremely high pressure, in this case 40 mm. of water, to overcome his pulmonary resistance. Since the lungs cannot withstand this amount of pressure long, I postulate a terminal bilateral pneumothorax.

Pulmonary Hypertension and Emphysema

What interests me most about this man is that his lung problems existed for over 30 years. Finally, his lung disease caused his heart to fail. Probably he had some type of pulmonary hypertension with right heart failure as a climactic event. Why pulmonary hypertension? He had polycythemia, apnea, characteristic x-rays, and right ventricular strain on the cardiogram. The usual cause for all of this is, of course, emphysema.

Obstructive emphysema produces pulmonary hypertension in different ways. Anoxic episodes play some role and so does fibrosis. Yet, though this man smoked three packs of cigarettes a day, his chest films show no emphysema.

Congenital and Acquired Heart Disease

Another group of disorders which can give rise to pulmonary hypertension includes congenital heart disease with shunts. He served two years in the Navy and was hospitalized to evaluate a tachycardia. It is unlikely that a man with congenital heart disease could slip by a team of Navy doctors without having a murmur detected. Also different examiners at St. Barnabas heard no murmur.

Acquired heart disease, such as mitral stenosis, can also produce pulmonary hypertension. Again the absence of murmurs effectively excludes this as cause of his problems. Certain facets of his illness, however, fit with mitral stenosis. These include paroxysmal tachycardia, pulmonary hypertension, and intractable failure. Also these patients have rales, become dyspneic and orthopneic, and can't lie down at night. But such symptoms are chronic and insidious in mitral patients, and this man didn't really get into trouble until the last week of his life. Then suddenly he went into complete right heart failure and never came out of it.

There are other rare disorders, such as *cor triatriatum*^{*}, which can act like this. But again most of those diseases produce murmurs, for shunts that give rise to cyanosis have murmurs.

Now I am approaching what I think this man had—primary pulmonary hypertension. What is primary pulmonary hypertension? Is it a disorder which is inherited? Is it the result of multiple pulmonary emboli? Patients with emboli can develop both pulmonary hypertension and heart failure.

The difficulty with that theory is that our patient's symptoms started when he

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^{*} See Test Your Word Score Page 1227.

was ten. Pulmonary emboli starting at ten in a man who worked as a laborer, who never had phlebitis, and who never coughed up blood are, in my opinion, unlikely. His course is more in keeping with primary pulmonary hypertension. He has the x-ray findings, the electrocardiographic changes, and the usual course. When he finally decompensated, he failed to respond to all measures.

In primary (or unexplained) pulmonary hypertension, patients are typically young. Their symptoms may start when they are four to six years old. But the usual onset of symptoms is in the third and fourth decade. The disease occurs in women four times more often than in men.

Polycythemia

That this patient was a man does not disturb me, but I find the elevated hemoglobin and hematocrit hard to explain. In theory, patients with primary pulmonary hypertension do not become polycythemic. But our patient suffered from anoxia for the last three months of life, probably even longer. Anoxia causes polycythemia, and I attribute his high hemoglobin and hematocrit to anoxia.

When a man with primary pulmonary hypertension becomes anoxic, his pulmonary arteries and arterioles constrict, the hypertension in the lesser circuit increases, and his vessels constrict still more. Once this cycle starts, it does not revert, and the patient goes on to fulminating death. Such a chain of events—pulmonary hypertension polycythemia, and sudden death—sometimes occurs in Peruvians who live at high altitudes.

The protocol does not list enough blood gas chemistries for me to discuss acid-base problems. He may have had a chronic CO_2 retention, but I doubt if he had the Pickwickian syndrome. That usually occurs in patients who are massively obese. This man was muscular, heavy, and edematous—not obese. He undoubtedly had respiratory acidosis and probably a carbon dioxide narcosis before he was given intermittent positive pressure breathing. When the machine began to exchange oxygen, readily diffusible carbon dioxide washed out, and a normal pCO_2 resulted. That he did not breathe on his own is good evidence for carbon-dioxide narcosis. His respiratory center failed to respond.

I am left with diagnoses of primary pulmonary hypertension, right ventricular hypertrophy, and pneumothorax.

Dr. Donald Bohn's Diagnosis

Primary Pulmonary Hypertension
Right Ventricular Hypertrophy
Pneumothorax

Discussion

Dr. William Renti-Cruz:*

If you suspected pulmonary hypertension, couldn't you document it by catheterizing the pulmonary artery?

Dr. Bohn:

Yes, but it's risky. These people die when you put a catheter in their pulmonary artery. Their vessels constrict further, they get arrhythmias, and they die. A catheterization would show normal wedge pressure, but a high pulmonary artery pressure.

*Intern, St. Barnabas Hospital.

Dr. Ramesh Kharwadkar:[°]

What about an angiogram?

Dr. Bohn

An angiogram would show a hypertrophic right ventricle, a dilated pulmonary artery, and large vessels disappearing at the periphery.

Dr. Liborio Liro:^{°°}

Could this be Ayerza's syndrome?

Dr. Bohn:

As far as I am concerned, this is Ayerza's syndrome. In 1901 Ayerza described a condition characterized by slowly developing bronchitis, dyspnea, cyanosis, and polycythemia. It is a primary disease of the pulmonary artery and its branches and has the same pathological findings as primary pulmonary hypertension.

Pathological Discussion

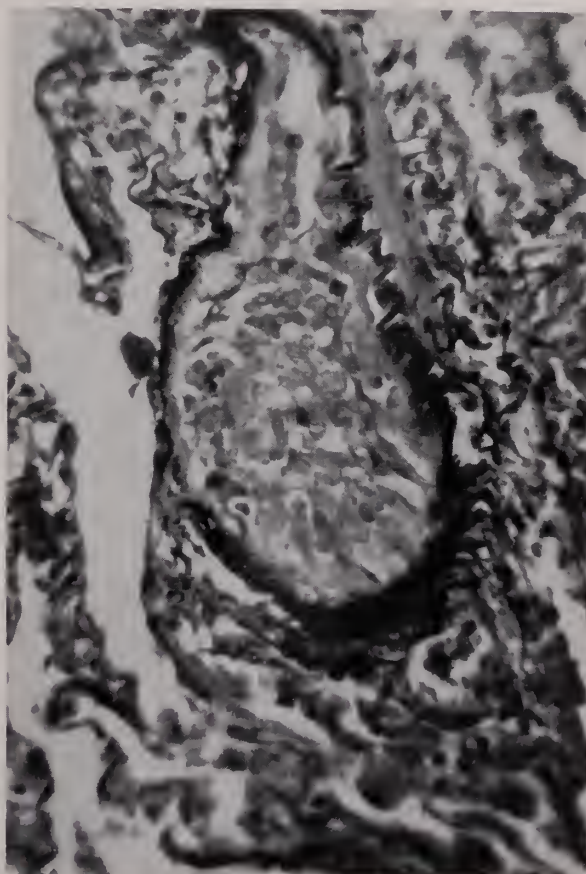
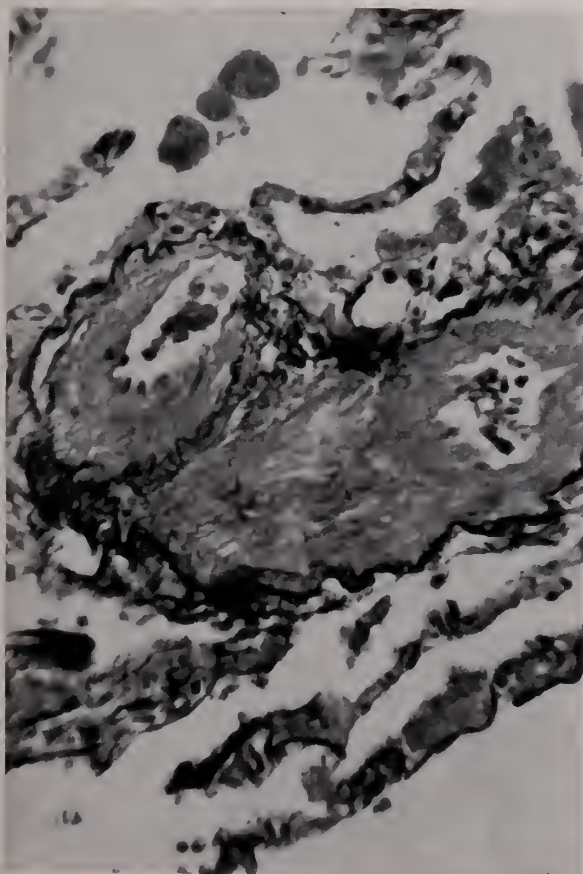
Dr. Richard Reece:[†]

Doctor Bohn hit the nail on the head. This man did have primary pulmonary hypertension with a pneumothorax. When I entered the chest cavity, air gushed

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Figures 1 (left) and 2 (right) — Photomicrographs of muscular arteries of lung showing intimal proliferation, hypertrophy of media, and prominent elastic laminae. $\times 430$ Verhoeff-Van Gieson.

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forth, and his diaphragms suddenly deflated. Although I looked for the precise source of his pneumothorax, I could not find it. I observed intact pleural blebs, but none were ruptured.

The right lung weighed 1000 grams and the left 550 grams. Though the lungs showed atelectasis, some lobes were consolidated and did not collapse. All lobes displayed a watery cut surface with froth exuding from the parenchyma and the bronchi. Microscopically, swarms of polymorphonuclear leucocytes crowded many alveolar spaces; the rest of the alveoli showed pulmonary edema and "heart failure" macrophages.

The pulmonary artery was dilated and sclerotic. Buttery arteriosclerotic plaques raised the intimal surface. Under the microscope, smaller pulmonary arteries and arterioles disclosed intimal endothelial proliferation, medial hypertrophy, and prominence of elastic laminae (Figures 1 and 2). These are the changes usually described in primary pulmonary hypertension.

The heart weighed 540 grams, and the right heart was hypertrophied and dilated. The wall of the right ventricle was more than one cm. thick. All the valves were delicate, and the coronary arteries were free of arteriosclerosis. The liver showed the changes of long-standing chronic passive congestion.

Final Anatomical Diagnoses

1. Dilatation of pulmonary artery with arteriosclerosis; intimal proliferation and median hypertrophy of pulmonary muscular arteries and arterioles (primary pulmonary hypertension)
2. Cardiomegaly (540 grams), right ventricular hypertrophy
3. Bilateral bronchopneumonia
4. Pleural blebs with bilateral pneumothorax (possibly secondary to intermittent positive pressure breathing)
5. Passive congestion of liver.

Richard Reece, M.D.
Minneapolis, Minnesota

Norman Code of Licensure (1140)

Who, from now on, wishes to practice medicine, has to present himself before our officials and examiners, in order to pass their judgment. Should he be bold enough to disregard this, he will be punished by imprisonment and confiscation of his entire property. In this way we are taking care that our subjects are not endangered by the inexperience of the physicians.

Nobody dare practice medicine unless he has been found fit by the convention of the Salernitan masters.

Editor's Note: Are our standards becoming less severe?

Books vs. Pictures

How much better it is to have the walls covered with books with which we are establishing friendly relations, than with pictures of passing interest which we happened to obtain. Eventually pictures lose their interest, whereas books never lose their fascination.—William Mayo

Cloxacillin for Prophylaxis in Oral Surgery

DANIEL E. WAITE, D.D.S.*
ALEXANDER SCHIRGER, M.D.**
WILLIAM J. MARTIN, M.D.**
Rochester, Minnesota

MEMBERS OF OUR group have previously reported data on the use of phenoxymethyl penicillin and erythromycin for the prevention of post-operative bacterial invasion of blood after oral surgical procedures.¹⁻³ In a continuation of these studies, sodium cloxacillin monohydrate, a penicillinase-resistant semisynthetic penicillin, was used. It is generally agreed that cloxacillin gives serum levels twice as high as oxacillin, when equal amounts of the drugs are given orally.⁴ The purpose of this study, as it has been with the others, was to test the effectiveness of the selected antibiotic agent under the conditions outlined.

Materials and Methods

The patients were selected solely on the basis of their need of oral surgical procedures. The surgical problems consisted mostly of impacted third molars and full-mouth extractions because of periodontal disease or caries or both. Sodium cloxacillin monohydrate† in capsule form was administered in four successive doses of 250 mg. beginning 18 hours prior to operation. Blood for cultures was drawn immediately after the operative procedure while the patient was still in the operating room and again approximately 18 hours later. Fifty-two patients were studied and no patient was included who had either pre-existing or known infection, valvular heart disease, or a combination of these problems. Ten of the 52 patients had positive cultures from the blood obtained immediately after the surgical procedure. As is apparent from the Table, cul-

tures of blood from nine of the 10 patients were negative 18 hours after operation. Cultures of blood from one of the other two patients showed an aerobic sporeformer in liquid medium only and cultures from the other patient showed *Streptococcus mitis*.

Comment

It is noteworthy that blood cultures in eight of the 52 patients yielded *Streptococcus mitis*. In seven cases, organisms were grown in samples of blood obtained immediately after operation; in the eighth case, blood was obtained 18 hours after operation. This high incidence approximates that encountered in one of our previous studies, wherein 50 patients did not receive any antibacterial agent before operation.¹ It stands in sharp contrast to our experience with patients who have received optimal amounts of phenoxymethyl penicillin^{1,3} or erythromycin⁵ before operation and in whom cultures for *Streptococcus mitis* have been consistently negative. The finding was not anticipated prior to the study, since cloxacillin is generally considered effective against streptococci of this variety. As a matter of fact, we had concluded a priori that the effect

Blood Cultures After Oral Operation With Cloxacillin
Administered Preoperatively (52 Patients)*

Positive cultures	Time after operation	
	Immediately	18 hours
<i>Streptococcus mitis</i>	7	1
<i>Staphylococcus coagulase-negative</i>	2	0
<i>Corynebacterium</i>	1	0
Aerobic sporeformer in liquid media	0	1

*Received 250 mg. every four hours for four doses.

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**Section of Medicine, Mayo Clinic and Mayo Foundation.

†Supplied as TegoPen, courtesy of Bristol Laboratories, Syracuse, N. Y.

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of cloxacillin would likely be similar to that of phenoxymethyl penicillin and erythromycin against most organisms inhabiting the oral cavity, and that its antistaphylococcal effect would be greater than that of these agents. However, even the latter effect is debatable, since blood cultures from two patients in the present series grew staphylococci in contrast to six of 94 patients receiving phenoxymethyl penicillin¹⁻³ and none of 42 receiving erythromycin.⁵ We chose cloxacillin rather than oxacillin because of the higher blood levels obtainable with the former drug. We are currently studying nafcillin, which results in blood levels comparable to those achievable with oxacillin, but concentrations of nafcillin appear to persist longer in blood and tissues.

From the data accumulated in the present study, it now appears necessary to give a group of patients 500 mg. of cloxacillin rather than 250 mg. and to determine the results in the manner described herein. If decreased intestinal absorption of cloxacillin were due to food ingested in the 18 hours before surgery, perhaps the increased dosage would result in higher serum levels and a more desirable antibacterial effect. In any event, we cannot recommend cloxacillin in the dosage employed in this study, in at-

tempts to prevent bacterial invasion of the blood after oral surgical procedures.

Summary

Fifty-two patients received cloxacillin in amounts of 250 mg. for four doses by the oral route beginning 18 hours before oral surgery. In 10 of the 52 patients, cultures of blood drawn immediately after operation grew bacteria. Seven of the 10 positive cultures grew streptococci of the *mitis* group and two grew coagulase-negative staphylococci. In an additional patient, cultures of blood drawn 18 hours after operation also grew *Streptococcus mitis*. These findings stand in sharp contrast to our experiences with patients who have received optimal amounts of phenoxymethyl penicillin or erythromycin preoperatively and in whom cultures for *Streptococcus mitis* have been consistently negative. Cloxacillin, in the dosage employed in this study, cannot be recommended in attempted prevention of bacterial invasion of the blood subsequent to oral surgical procedures.

Acknowledgement

The authors wish to express appreciation to G. M. Needham, Ph.D., of the Section of Microbiology for his assistance in this study.

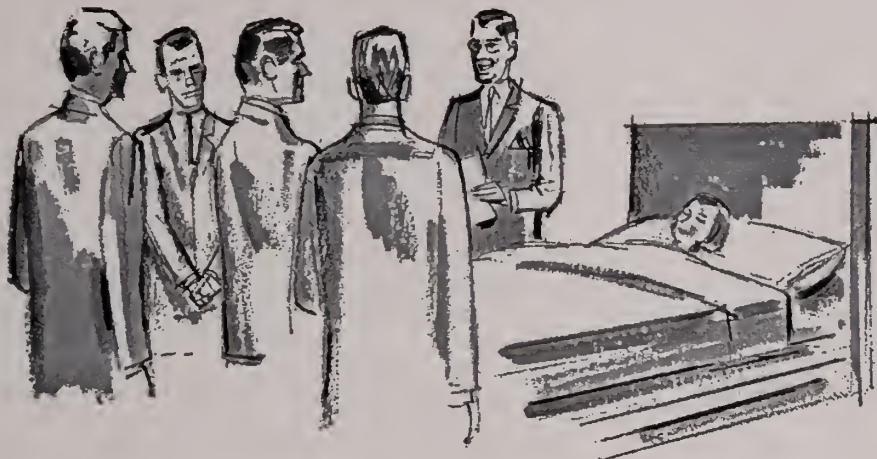
References

1. Schirger, A., Martin, W. J., Royer, R. Q., and Needham, G. M.: Bacterial Invasion of Blood After Oral Surgical Procedures. *J Lab Clin Med* 55:376, 1960.
2. Martin, W. J., and Schirger, A.: Prevention of Bacteremia After Oral Surgery. *Minnesota Med* 47:1519, 1964.
3. Schirger, A., Martin, W. J., Royer, R. Q., and Needham, G. M.: Phenoxymethylpenicillin (Penicillin V) for Prophylaxis Prior to Oral Surgery in Patients With Heart Murmurs. *Mayo Clin Proc* 39:359, 1964.
4. Martin, W. J.: Newer Antimicrobial Agents Having Current or Potential Clinical Application. *Med Clin N Amer* 48:255, 1964.
5. Schirger, A., Waite, D. E., and Martin, W. J.: Erythromycin for Prophylaxis Prior to Oral Surgery in Patients Allergic to Penicillin. (In press.)

Music and Disease

I ran across the statement very recently in the book of Theophrastus On Inspiration that when gouty pains in the hips are most severe they are relieved if a flute-player plays soothing measures. That snake bites are cured by the music of the flute, when played skillfully and melodiously, is also stated in a book of Democritus entitled On Deadly Infections, in which he shows that the music of the flute is medicine for many ills that flesh is heir to. So very close is the connection between the bodies and the minds of men, and therefore between physical and mental ailments and their remedies.

—Aulus Gellius (2nd Century A.D.)



Grand Rounds

Acute Benign Pericarditis*

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Medical Resident

THE SUBJECT of this paper is misleadingly called "benign" since, in some instances, the complications are life-threatening. The term pericarditis is pathologically too limiting because in every recognizable instance there is also myocardial involvement. Even the term "acute" is less than truthful, for frequency of recurrence is one of the common findings in the disease. Acute benign pericarditis is a non-specific form of acute serofibrinous pericarditis, which may be caused by a variety of etiologic agents. Pericarditis is, of course, an inflammation of the membranes which envelop the heart. However, the symptoms and signs and the laboratory data in acute pericarditis cannot be explained by pathology of the pericardium alone. Most of the laboratory and clinical manifestations are secondary to involvement of the lungs, pleura, epicardium, myocardium and conduction system of the heart.

One of the more common varieties of acute pericarditis is that cluster of diseases called acute benign pericarditis, acute idiopathic or acute non-specific pericarditis. None of these names is free from objection, and one author has suggested "acute perimyocarditis" as a more suitable name⁴. Acute benign pericarditis has been historically a wastebasket diagnosis. As specific etiologies for more and more forms of acute pericarditis have been delineated, the "idiopathic" spectrum has narrowed. A wide variety of forms of pericarditis, including Dressler's syndrome, post-pericardiotomy syndrome, and post-traumatic pericarditis, are very similar clinically to acute benign pericarditis and were certainly contained in the wastebasket of acute benign pericarditis at one time. The pericarditis associated with systemic lupus erythematosus was also retrieved only relatively recently.

Etiology

In the recent literature acute benign pericarditis has been attributed to either a viral infection or a hypersensitivity reaction or to combinations of both. The case for a viral etiology has been well established by numerous investigators^{17,18,19,20}.

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, January 17, 1967.

Continued

Virus

Coxsackie B, types 2, 3, 4, and 5, have been implicated in most reported cases associated with a virus. Many investigators have recovered the virus in stool specimens obtained during the illness, and by demonstrating a rise in the titer of neutralizing antibodies obtained in acute and convalescent sera. In a few cases the virus has been isolated by pericardial fluid aspiration. Other viruses implicated have been influenza A and B^{9,14}, mumps²¹, Echo type 8²¹, infectious mononucleosis¹⁵, and chickenpox. None of these viruses have any myocardial or pericardial specificity, and it is probable that any viral infection may occasionally produce acute benign pericarditis. Spink et al.⁸ stated that myocarditis complicated upper respiratory infections in 10.8 percent of cases. Another study of an epidemic of Coxsackie virus infections showed three patients out of 28 to have myocardial and pericardial involvement¹⁶.

Idiopathic

Despite the recent emphasis on viral etiology of acute benign pericarditis, many cases must still be considered idiopathic. One study reviewed 34 cases of acute benign pericarditis in which exhaustive investigations were performed in search of a specific etiologic agent, and in only five cases were viruses implicated²¹. Another series of 269 cases reported preceding upper respiratory infections in only about 30 per cent of patients³.

Anti-Heart Antibodies

There has been speculation that some cases of acute benign pericarditis may be secondary to an allergic, auto-immune, or hypersensitivity process. It has been mentioned that the syndrome of acute benign pericarditis is very similar to Dressler's syndrome and to the post-pericardiotomy syndrome. There may be an identical non-specific immunologic response due to many agents causing myocardial and pericardial injury. In Dressler's syndrome, post-pericardiotomy and post-trauma syndromes, the initial injury to the myocardium alters a myocardial protein which becomes an antigen, to which the heart develops anti-heart antibodies. By means of the indirect immunofluorescence technique and the anti-globulin-consumption test, antiheart antibodies have been detected in 13 of 15 cases of post-pericardiotomy syndrome and in eight of 14 cases of Dressler's post-myocardial infarction syndrome²². It may be that in some cases, mild viral infections have caused myocardial or pericardial injury, following which the heart develops anti-heart antibodies, but this has not been demonstrated to be the case in acute benign pericarditis. However, no thorough study has been made of a large group of acute benign pericarditis patients in an attempt to demonstrate anti-heart antibodies.

We are left with two major groups in consideration of the etiology of acute benign pericarditis: first, the viral agents, which some authors set aside as acute viral pericarditis, but which most authors lump with the "benign" or "non-specific" category; secondly, the larger, but clinically indistinguishable group of "idiopathic" etiology.

Clinical Features*Chest Pain*

Acute benign pericarditis is frequently associated with or preceded by an upper respiratory infection. The onset is usually acute, heralded by the sudden

ACUTE BENIGN PERICARDITIS

appearance of chest pain, usually substernal, of any intensity, radiating into the neck or shoulder but seldom down the left arm. However, Barnes and Burchell reported 14 cases of "acute pericarditis simulating acute coronary occlusion."²³

Epigastric Pain

Abdominal laparotomies have been performed because of the location of the pain in the epigastrium. The pain is often increased by deep inspiration and by recumbency, especially in the left lateral decubitus position. Coughing and swallowing may aggravate the pain. It is often relieved by sitting up and leaning forward. The pain in pericarditis is probably produced by either or both of the following: (1) Distention of the pericardial sac by effusion with stimulation of the only pain-sensitive portion of the pericardium, the lower parietal pericardium. This is often a dull aching pain. (2) An associated pleuritis involving the pleura adjacent to the pericardium, which would account for the sharp pain and radiation from the substernal area.¹

Fever

Fever is a frequent finding, often in the range of 101 to 103 degrees F. Dyspnea is a prominent symptom, usually manifested by a rapid respiratory rate and shallow forced respirations. The pathogenesis of the dyspnea is unknown. A pericardial friction rub is present at some time in most cases. Pleural and pericardial effusions are common. It must be remembered that although a pericardial friction rub is pathognomonic, it is by no means essential to the diagnosis. Atrial arrhythmias may occur but are infrequent.

TABLE
Clinical Data on 34 Patients with Acute Benign Pericarditis²¹
Frequency in Percent

<i>Symptoms</i>	
Pain	100
Dyspnea	32
URI	24
Nausea and vomiting	15
<i>Signs</i>	
Fever greater than 100 degrees F.	82
Pericardial friction rub	62
Tachycardia	16
Rales	15
Pharyngitis	12
Lymphadenopathy	12
Pleural friction rub	12
<i>Laboratory Results</i>	
EKG abnormalities	97
Characteristic S-T and T wave changes	79
T wave changes without S-T elevations	15
Non-specific changes	3
Abnormal chest x-rays	59
Enlarged cardiac silhouette	41
Pleural effusion	18
Parenchymal infiltrate	15
Leukocytosis greater than 10,000	59

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Electrocardiogram

The electrocardiogram is frequently but not always abnormal in cases of acute pericarditis, and the changes observed are suggestive rather than diagnostic of pericarditis. Because of the non-specific nature of the changes, one cannot use the electrocardiogram in acute pericarditis to differentiate between acute benign pericarditis and other forms of acute pericarditis. The common electrocardiographic changes observed in acute pericarditis were found in 80 per cent of 57 cases in one study,¹⁰ while another group found 61 per cent of 76 cases¹¹ to have the characteristic abnormalities. Hull,¹² in an excellent symposium on pericarditis, stresses that none of the electrocardiographic changes commonly associated with pericarditis are directly due to involvement of pericardial membranes per se. It is probable that most cases which lead to changes in the electrocardiogram and in all cases where the typical changes are manifest, the process is diffuse, involving most or all of the epicardium.¹²

S-T Segment

S-T segment elevation is thought to be secondary to diffuse subepicardial myocardial injury.¹⁰ S-T segment elevation is usually the earliest electrocardiographic abnormality seen in acute benign pericarditis and often disappears with early clinical improvement. Typically an upward concavity of the S-T segment is seen, and in early cases T waves of normal form evolve from it, in contradistinction to the usual convexity of the S-T segment elevation seen in acute myocardial infarctions. Also missing is the usual reciprocal S-T depression seen in myocardial infarctions. In many cases of acute pericarditis AVR and V₁ remain unaffected.

T Wave

T wave changes are usually found later in the course, and in the more "benign" cases may never appear.¹³ Most frequently the T waves flatten progressively as the S-T segment returns to the isoelectric line. This may occur in days or weeks. T wave inversion may occur without S-T changes preceding it and, although with the passage of weeks or months the T waves usually become upright and of full amplitude, permanent inversion or diminished amplitude is not infrequent. The S-T segment and T wave may change from day to day and from lead to lead. The instability of these electrical changes is in itself suggestive of a diagnosis of acute pericarditis.

QRS Complex

In cases where a pericardial effusion complicates the picture of acute benign pericarditis, decreased amplitude of the QRS complex is frequently seen. It must be emphasized that in a considerable percentage of effusions, even large ones, there will be no diminution of the QRS voltage. In addition, low voltage is seen in a considerable number of other conditions: for example, those in which there is fluid accumulation such as pleural effusion and metabolic disorders of the myocardium. The low voltage seen with diffuse myocardial disease may closely resemble that of a pericardial effusion. Suffice it to say that the electrocardiogram plays a minor role in the diagnosis of pericardial effusion.

Arrhythmias are infrequently associated with pericarditis, but they have been noted in cases of acute benign pericarditis of viral origin.¹ The usual picture is atrial fibrillation.¹³ It may be that the superficial location of the sinus node

less than 1 mm. beneath the epicardium is a factor in the production of atrial arrhythmias.

Complications

Complications of acute benign pericarditis include effusion, with or without tamponade, hemopericardium, chronic constrictive pericarditis, and repeated recurrences, although effusion and recurrence have been reported as occurring frequently with this disease.

Constrictive Pericarditis

Chronic constrictive pericarditis is generally thought to be a rare sequel of acute benign pericarditis.⁶ Review of the literature of long-term follow-up studies on 522 patients with acute benign pericarditis revealed that six had developed constrictive pericarditis.⁵ There have been 11 reported cases of chronic constrictive pericarditis following acute benign pericarditis. Of these, six developed constriction within six months and the remainder within four years of the acute episode.⁵ It has been pointed out⁵ that studies of patients with chronic constrictive pericarditis reveal a large percentage of cases of unknown etiology. This suggests the possibility that some of these cases may have followed acute benign pericarditis. I would interpret this data to indicate that although constriction is an uncommon complication and sequel to acute benign pericarditis, it is more frequently found than has been appreciated.

Effusion

In a large study³ approximately 35 per cent of the patients developed significant effusions, a diagnosis made largely on roentgenographic evidence. In general the patients with effusion were felt to have a more severe form of the disease, as evidenced by more pain, a prolonged course, and especially the increased incidence of recurrence. There was a 40 per cent recurrence rate in patients with effusion, versus a 15 per cent recurrence rate in those patients without effusion. Another group²¹ had pericardial effusions demonstrated in 41 per cent of patients, and had pleural or pneumonic manifestations in 32 per cent. The overall recurrence rate appears to be about 20 to 25 per cent, with the higher rate expected in patients with effusion.

Cardiac Tamponade

Twelve fatalities have been reported in patients with acute benign pericarditis.⁷ In five cases, cardiac tamponade was present and was thought to be the cause of death. In four of these cases, anticoagulants had been administered and the fluid was sanguinous. The remainder of the cases were associated with various forms of underlying myocardial disease. It would appear that when acute "benign" pericarditis occurs in a patient with some pre-existing moderately severe myocardial disease, the disease is no longer "benign."

Diagnosis and Differential Diagnosis

Sodeman and Smith report only 20 per cent accuracy in the recognition and diagnosis of acute pericarditis.²⁵ As is true in so many conditions, a high index of suspicion is necessary to make the correct diagnosis. The differential diagnosis is essentially that of chest pain.

Continued

Myocardial Infarction

Myocardial infarction is the most important diagnosis to exclude because of the prognosis and therapy. This is especially important in this era of anti-coagulants. The presence of a friction rub early in the course, pericardial effusion, the nature of the chest pain, characteristic electrocardiogram changes, presence of fever and preceding or concomitant upper respiratory infection help distinguish pericarditis from myocardial infarction. The level of the serum glutamic oxaloacetic transaminase may be helpful, but increased levels may be found in pericarditis. As one might expect, the serum glutamic oxaloacetic transaminase elevation has been shown to be related to the extent of subepicardial injury rather than the magnitude of pericardial inflammation.²⁴

Pulmonary Disease

Pneumonia and pulmonary infarction are also likely to be confused with acute pericarditis. Routine work-up should include complete blood cell count, urinalysis, blood cultures, sedimentation rate, electrocardiogram, chest x-rays, skin tests for TBC and triple fungus, and viral studies.

Diagnosis of pericarditis per se is not adequate. One must rule out all of the other causes of acute pericarditis before diagnosing acute benign pericarditis. Bacterial (especially tuberculous), neoplastic, metabolic, traumatic, and allergic etiologies must be ruled out. In addition, the S.L.E., rheumatic fever group of collagen-hypersensitivity diseases must be excluded. Even if presumptive laboratory findings indicate a viral etiology, the other causes must be ruled out, since viral infections may coexist with, but not be the cause of pericarditis of another origin. Some authors urge pericardial biopsy and/or diagnostic aspiration of pericardial fluid if the diagnosis remains in doubt. Lupus erythematosus cells should be searched for diligently, especially in young females.

Treatment*Bed Rest*

Complete bed rest is the best treatment for acute benign pericarditis, and in most patients the early institution of bed rest alone results in the prompt subsidence of symptoms. Usually a total period of two to three weeks is sufficient, but bed rest should be continued beyond the time of disappearance of any friction rub. If temperature elevation or chest pain recurs, bed rest should be reinstituted. Most cases will require only mild analgesics such as salicylates; when pain severe enough to require opiates is present, it will usually be unnecessary to continue them beyond the first few days of hospitalization. Antibiotics are of no benefit in this type of pericarditis.⁴

Steroid Therapy

Corticosteroids have proven to be of particular value in the relief of pain when opiates are ineffective. They also lessen the dyspnea associated with splinting of the chest without the impairment of ventilation which may be seen with opiates. The dosage usually recommended is from 40 to 80 mg. of prednisone daily in four divided oral doses.^{1,2,4} In critically-ill patients the response is often dramatic, with relief of symptoms in less than 24 hours. When the patient is afebrile and symptom-free, the dose should be cut to 20 mg. per day and then gradually reduced over the next two or three weeks. If difficulty is encountered in termination of the course of steroids, addition of analgesics may prove helpful.

It is the impression of some investigators that steroids may decrease the formation of pericardial fluid and the likelihood of pericardial tamponade. There are no data to suggest that the course of an attack of acute benign pericarditis is shortened by steroid therapy, and the premature withdrawal of steroids often results in a "rebound phenomenon" with return of pain and fever.² It cannot be overemphasized that steroids must be reserved for those who are severely ill and do not respond to other measures. In one series of 27 patients with acute benign pericarditis complicated by recurrences, 67 per cent had good response to a regimen of steroids brief in duration and moderate in dosage. However, the remaining 33 per cent had repeated rebound phenomena associated with cessation and required up to three years for withdrawal.³ Bacterial and especially tuberculous pericarditis must be vigorously sought and ruled out before steroids are instituted. There has been no evidence that viral illness might be disseminated by steroid therapy.²

Operative Procedures

Pericardiocentesis is probably more often done for diagnostic than for therapeutic reasons, but if there is evidence of cardiac tamponade a vigorous rather than expectant course of action is indicated.¹

Pericardiectomy is usually reserved for patients with chronic constrictive pericarditis, a rare complication of acute benign pericarditis, and should be given serious consideration in the presence of recurrent pericarditis to prevent further recurrences.³

Case Report

A 21-year-old white single male, a college student, was admitted to this hospital on 9/18/66 with a chief complaint of chest pain. He dated the onset of his present illness to four days prior to admission, when he developed a "cold," sore throat, back pain, slight dysuria and increased frequency. Within 24 hours he had chills and a temperature of 103 degrees F.

He presented himself to the Hennepin County General Hospital emergency room on 9/15/66. Erythema of the throat and CVA tenderness were noted. Wbc. was 16,300 with 82 P.M.N.'s. Throat culture obtained eventually grew "normal flora." Urinalysis showed only occasional wbc.'s and was negative for albumin. Urine culture was "no growth." Despite the lack of positive findings he was treated with gantrisin for a urinary tract infection. The following day his throat was red and he was treated with I.M. Bicillin. On 9/17/66 he noted the onset of chest pain for the first time. He described it as gradual in onset, substernal, non-radiating, non-pleuritic, and lasting approximately 45 minutes, disappearing spontaneously. He denied cough or dyspnea. On the day of admission, he was awakened at 4:30 a.m. by a similar type of pain, this time accompanied by diaphoresis. Seen in the emergency room two hours later he still complained of chest pain. His temperature was 101 degrees F. Urinalysis and complete blood count were normal; sedimentation rate was 22. He was sent home but returned a few hours later because of the recurrence of very severe substernal non-radiating chest pain. He appeared pale and acutely ill; his blood pressure was 100/60. He was admitted after an electrocardiogram was obtained.

Physical examination on admission revealed, in addition, bilateral white tonsillar exudates. No pleural or pericardial friction rubs were heard. The remainder of the physical examination was within normal limits.

Hospital Course

The initial electrocardiogram showed S-T segment elevation in leads II, III, and AVF. Serum glutamic oxaloacetic transaminase obtained consecutively were 95, 53, 23, 12, and remained normal thereafter. Sedimentation rates were 22, 34, 79, 79, 21, 11, and 5. L.E. preps were negative. Heterophile titers were negative. C.b.c.'s were within normal limits throughout the remainder of the hospital course. The patient had one episode of chest pain, relieved by demerol, after admission. He became afebrile shortly after admission and

Continued

GRAND ROUNDS

remained so. Fungal and TBC skin tests were negative. By 9/20/66 the electrocardiogram showed S-T segment elevation and terminal T negativity in I, AVL and V6. By 9/26/66 the S-T elevation returned to the baseline and the T waves become more negative. The patient was discharged on 9/27/66. Discharge diagnosis: Acute benign pericarditis, viral etiology suspected, not proven.

Follow-up electrocardiogram on 10/11/66 showed negative T waves in I, II, III, AVF, V5 and V6. Follow-up electrocardiogram on 1/4/67 showed all negative T waves returned to upright position.

References

1. Friedberg, C. K.: Diseases of the Heart. W. B. Saunders & Co., 1966.
2. Logue, B., and Tutunji, F.: Amer Heart J 64:570, 1962.
3. Connolly, D. C., and Burchell, H. B.: Amer J Cardiol 7:7, 1961.
4. Bradley, E. C.: Amer Heart J 67:121, 1964.
5. Azar, G. J.: Amer Heart J 65:474, 1963.
6. Wood, P.: Amer J Cardiol 7:48, 1961.
7. Liu, H. Y., and Garcia, R.: Amer Heart J 69:677, 1965.
8. Rantz, L., Boisvert, P. J., and Spink, W.: Arch Intern Med 76:131, 1945.
9. Adams, C. W.: Amer J Cardiol 4:56, 1959.
10. Bellet, S., and McMillan, T. M.: Arch Intern Med 61:381, 1938.
- 11-25. May be secured from Grand Rounds Editor

The Mithridaticum

Mithridates lived in constant fear of being poisoned, to overcome which, he tested a large number of poisons on criminals and prisoners of war, and took small, increasing doses of poisons and antidotes during the greater part of his life. Today we use the term mithridatism in medicine to denote the insusceptibility to the effects of poison produced by taking a series of gradually increasing doses . . . When Pompey defeated Mithridates (66 B.C.) he found the prescription for this very complex general antidote, together with other medical manuscripts with the king's body. This famous prescription became known as the Mithridaticum.

The mithridaticum was improved especially by Nero's personal physicians and its use extended to a great number of ailments. There were two principal formulas named for Nero's physicians respectively, one having fifty-five ingredients, and the other seventy-two. In Nero's time these complex prescriptions became known as Theriacs, the word being derived from the snake called tyrus, the flesh of which was added to the ingredients by Andromachus, Nero's doctor. Directions for making theriacs are to be found in all dispensaries down to those of the 19th century.*

*Thomen, A.A., M.D.: Don't Believe It! Says the Doctor. Blue Ribbon Books, New York, 1935.

Many persons think they have open minds; actually their minds are just vacant.
—Wingspread



Abstracts, Briefs and Commentaries

BREAST CARCINOMA

Goldsmith et al. have studied a series of consecutive autopsies on women who had been operated on for carcinoma of the breast. They were particularly interested in the pulmonary lymphangitic metastasis which occurred and found that approximately 25% of the post-mortem examinations reveal pulmonary lymphangitic involvement and that approximately 20% died a pulmonary death.

Not all of these pulmonary lymphangitic involvements were demonstrable by Xray. The restrictive lung disease symptoms caused by the pulmonary lymphatic metastases were evidenced in decreased tidal volume, increased rate of frequency, diminished inspiratory capacity and vital capacity, and diminished maximum breathing capacity and reserve volume. The only other pulmonary state that can give a comparable set of pulmonary function abnormalities is thought to be a radiation fibrosis.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Goldsmith, Bailey, Callahan, and Beattie: Pulmonary Lymphangitic Metastases from Breast Carcinoma. Arch Surg 94:483, 1967.

MELANOMAS OF THE VAGINA

Melanomas are migratory marauders and can crop up anywhere in the body where melanocytes exist. About 3 per cent of vaginas have intraepithelial melanocytes, and three dozen melanomas have been reported to arise there. Norris and Taylor, pathologists at the Armed Forces Institute of Pathology, review 13 cases. The melanomas presented as soft, blue-black, bleeding masses in older women (average age 62 years). The median survival after surgery was 10 months. Ten of the 11 patients surviving more than one year died of metastases, and one still lives, more than six years after surgery. Norris and Taylor documented melanomic pigment in 11 lesions and functional change in 10. Five tumors displayed spindle cell transformation, and two were comprised of anaplastic cells indistinguishable from anaplastic carcinoma or lymphoma. Pathologists confronted with an undifferentiated vaginal neoplasm should search for pigment and functional change to make a clear-cut diagnosis. Nearly all pigmented vaginal lesions are malignant.

Richard Reece, M.D.
Minneapolis, Minnesota

Norris, H. J. and Taylor, H. B.: Melanomas of the Vagina. American J Clin Path 46:420, 1966.

TREATMENT OF HYPERTHYROIDISM

In recent years the treatment of hyperthyroidism has been both surgical and medical. The medical treatment consists principally of radioactive iodine or antithyroid drugs.

Plested and Pollock of the University of California, Los Angeles, have made a comparison of the end results of surgical vs. medical management. In their studies the surgical management produced a euthyroid state in 87%, whereas management with radioactive iodine provided 71% benefit. More significant might be the incidence of hypothyroidism in the two series, in which the surgically operated patients developed a 5% incidence of hypothyroidism whereas the radioactive iodine-treated patients developed a 20% incidence.

The authors were able to conclude that under modern conditions sub-total thyroidectomy is still a good and safe form of therapy for hyperthyroidism, resulting in fewer long-term complications than any other method presently available.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Plested and Pollock: Radioactive Iodine, Anti-Thyroid Drugs and Surgery in Treatment of Hyperthyroidism. Arch Surg 94:517, 1967.

FORECASTING THE SEX OF THE UNBORN CHILD

Given a long needle, a bottle of cresyl violet stain, some alcohol, and a microscope, one can predict the sex of a fetus in the uterus with 100 per cent accuracy. Doctors A. P. Amarose, A. J. Wallingford, and E. J. Plotz of the Albany Medical College report that a cytogeneticist* and three technicians correctly forecast the sex of 31 unborn children by studying amniotic fluid from Rh-negative sensitized women. In fetal cells from males, examiners see no sex-chromatin bodies. Twenty to 40 per cent of females have a sex-chromatin mass. Removing fluid from the amniotic sac can be dangerous and should not be used to satisfy the curiosity of expectant patients, but physicians who have reason to diagnose sex-linked hereditary diseases may want to use the technique as a tool in preventative genetics.

Richard Reece, M.D.
Minneapolis, Minnesota

* See Test Your Word Score Page 1227.

Amarose, A. P., Wallingford, A. J., and Plotz, E. J.: Prediction of Fetal Sex from Cytological Examination of Amniotic Fluid. New Engl J Med 275:715, 1966.

DISEASES OF BRAIN AND ABDOMEN AND PH

Before the advent of pH. measurement, most physicians relied on the CO₂ content as an indicator of acid-base imbalance. Dr. Gambino, clinical pathologist at Englewood Hospital in New Jersey, exposes the hazards of this approach. He presents nine patients who had normal carbon dioxide levels but who showed pH.s ranging from 7.51 to 7.59. Each patient had a serious intracerebral or intraabdominal disease. Dr. Gambino calls the combination of an elevated pH. and normal CO₂ "unsuspected venous alkalemia," and says it is frequent in patients with peritonitis, ascites, liver coma, and hypertensive encephalopathy.

Richard Reece, M.D.
Minneapolis, Minnesota

Gambino, R. S.: Unsuspected Venous Alkalemia—A Laboratory Sign of Serious Disease. JAMA 198:484, 1966.

BILATERAL CARCINOMA OF THE BREAST

Bilateral carcinoma of the breast is thought to occur at an incidence rate of about 6.5%. This is not necessarily simultaneous but occurs during the life of the individual. Simultaneous carcinoma occurred in about 1%.

The authors pointed out that some authorities therefore have recommended simple mastectomy on the uninvolved side.

Carl O. Rice, M.D.
Minneapolis, Minnesota

Shellito and Bartlett: Bilateral Carcinoma of the Breast. Arch Surg 94:489, 1967.

PERNICIOUS ANEMIA IN CHILDHOOD

The prototype for pernicious anemia: a middle-aged or elderly patient with gray hair, blue eyes, lemon skin and neurological difficulty, is so much a part of medical lore that many doctors do not think of the disease in children. Yet two types of pernicious anemia exist in childhood: the adult type with gastric atrophy and the juvenile congenital type with congenital lack of the intrinsic factor and no abnormality of the stomach and its secretions.

Miller and his colleagues from the Harvard Medical School present three male infants who had onset of pernicious anemia at eight months, nine months and seventeen months. All had low levels of serum B₁₂, megaloblastic anemia, and absent intrinsic factor with normal gastric secretion and normal gastric mucosal histology. The intrinsic factor corrected the absorption defect in all children, and the histology remained normal five, eleven and twenty-nine years after intrinsic B₁₂ or liver extract therapy. The investigators studied 43 relatives and found no increased incidence of intrinsic factor or parietal cell antibodies, both common in patients with adult pernicious anemia. Childhood pernicious anemia, they conclude, does not predispose to gastric atrophy.

Richard Reece, M.D.
Minneapolis, Minnesota

Miller, D. R., Bloom, G. E., Streitt, R. R., LoBuglio, A. F., and Diamond, L. K.: Juvenile Congenital Pernicious Anemia. New Engl J Med 275:978, 1966.

BLOOD CLOTTING AND THE PILL

Doctors started to prescribe contraceptive drugs to the public in 1960. Although several blue ribbon committees, including one supported by the Federal Drug Administration, declared the drugs safe, the literature abounds with reports of thrombophlebitis and pulmonary emboli; and lingering doubts about the safety of the drug remain. Poller and Thomson of the Eithington Hospital in Manchester, England, studied the effects of oral contraceptives on clotting in a large group of women taking a variety of commercial preparations. Nearly all subjects showed a significant increase in Factor VII Level after they had received drugs for three months. The investigators also detected elevated Factor VII Levels in pregnant patients, post-partum females and individuals with deep thrombosis. Potter and Thomson conclude that the Factor VII increase is an undesirable side effect of oral contraception, and doctors should use drugs discretely for limited time periods.

Richard Reece, M.D.
Minneapolis, Minnesota

Poller, L. and Thomson, J. M.: Oral Contraceptive Hormone and Blood Coagulability. Brit Med J 2:23, 1966.

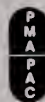
The best time to loaf is after you're dead.—Forbes Epigrams

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Book Reviews

When a book raises your spirit, and inspires you with noble and manly thoughts, seek for no other test of its excellence.—It is good, and made by a good workman.

—Bruyere

THE PEDIATRICIAN'S OPHTHALMOLOGY—Edited by Sumner D. Liebman, M.D., and Sydney S. Gillis, M.D., St. Louis, C. V. Mosby Co., 1966. 337 pages, 120 illustrations, 7 color plates, chapter references, index. Price: \$19.50.

This comprehensive book is, to the reviewer's knowledge, the best available in the interesting area of eye conditions of children, especially as they fit into the various syndromes. It is the result of well edited contributions of 25 authors covering 19 subjects. Both as fascinating reading as well as organized and detailed reference material it should be in the library of the pediatrician and the ophthalmologist. There is a useful table of inherited syndromes as well as a glossary of ophthalmic language. In the section on reading disability, the complexity of diagnostic terms and the brevity of the discussion on treatment underline the real lack of knowledge in this distressing area. From the reviewer's personal experience, this book should be read before taking the American Board of Ophthalmology.

William S. McClanahan, M.D.
Meriden, Connecticut

MENTAL RETARDATION — A Family Study by Elizabeth W. Reed, Ph.D. and Sheldon C. Reed, Ph.D. W. B. Saunders Company, Philadelphia and London, 1965. 716 pp.

Anyone who counsels or treats a mentally subnormal individual needs this book. It is not only an excellent resource for genetic counseling, but also a thorough and objective investigation of mental subnormality. To achieve their goals the authors examined data on the mental status, economic, educational, and social achievements of 82,217 persons. All of these persons were in some way related to 289 patients hospitalized at the Faribault State School for The Retarded between 1911 and 1918. By a careful compilation and evaluation of this material the authors unquestionably prove the following:

(1) The greatest predisposing factor for the appearance of mental retardation is the presence of retardation in one or more relatives.

(2) Cultural deprivation may lower the intellectual performance of any person, but if the polygenetic theory

of intelligence is valid there is little opportunity for cultural deficiencies to be the primary cause of retardation.

(3) When voluntary sterilization for the retarded becomes part of the culture of the United States, we should expect a decrease of about 50% per generation in the number of retarded persons as a result of all methods combined to reduce retardation.

The above conclusions are only a few of the provocative and interesting ones found in this book. Those inclined to emotional thinking will undoubtedly deny many of these conclusions, yet the evidence offered by the authors is compelling. The book is a long one, but the meat of it is in the first 79 pages. The remaining 637 pages consist of an elaborate and detailed appendix including a pedigree of all persons studied. Throughout the book, one is impressed with the crisp literary style and lack of jargon. All told, the book is excellent in every respect, and belongs on many bookshelves.

James Janecek, M.D.
St. Paul, Minnesota

SURGICAL DISEASES OF THE CHEST — Edited by Brian Blades. Second Edition 9/66, \$25.00. C. V. Mosby.

This is a fine text covering a rather extensive field. The major change from the previous edition has been in the sections dealing with cardiac abnormalities and their surgical correction. The rapidly changing field of cardiovascular chest surgery almost precludes any text from being completely current, and this applies to this effort. However, by the same token, current procedures now popular that will soon be phased out of practice are avoided.

The book contains 687 pages with a good bibliography at the end of each chapter section. There are chapters covering basic thoracic physiology and postoperative care of the thoracic surgical patient. Chapters on extra corporeal circulation and hypothermia, anesthesia, and ancillary procedures such as bronchoscopy and esophagoscopy are included.

The surgical trainee should find the book particularly valuable, and to those advanced physicians with a special interest in this field it will provide a good reference source.

Harrison H. Farley, M.D.
Minneapolis Minnesota



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Athletic Injuries

Preseason Conditioning Exercises For High School Football Players^{*}

EDWARD D. HENDERSON, M.D., Chairman
DONALD J. ERICKSON M.D.
Rochester, Minnesota

MANY PHYSICIANS and coaches have long recognized the need for preseason conditioning before participation in competitive sports by both high school and college athletes as one means of reducing the incidence of injuries. The report by Honet and associates¹ showed that various aspects of physical fitness require several months of conditioning exercises for optimal development. Preconditioning was associated with an increase in maximal work output during the first two months of participation in high school football, whereas the control group (nonconditioned) showed a decline in maximal work output: results which indicated a need to reevaluate the effectiveness of the present system of training prior to the commencement of the football season. Other studies² have also shown that various aspects of physical fitness require at least several months of conditioning for optimal development.

Conflicting Rules

The National Federation of State High School Athletic Associations has recommended a period of several months of conditioning exercises prior to the onset of the athletic season.¹ However, this recommendation may be carried out in Minnesota only at the expense of violating the rules of the Minnesota State High School League as published in the official handbook:³

1. Practice may begin two (2) weeks prior to the first Monday in September.

2. Practice and the season will be terminated upon completion of the final game on the Official Schedule for each school.

3. No school may engage in any football game or games, practice, training or other football activities between the close of one season and the opening of the next season. . . . This regulation includes conditioning, training, or instruction conducted directly or indirectly by school officials or other interested individuals with the exception of the secondary students.

4. For practice sessions, the handbook states that two (2) weeks of organized practice ". . . must precede the first game. . . . nine (9) separate and complete days of practice must be held before school engages in interscholastic games." In addition: "Inter-school practice scrimmages may not be held until after five (5) separate and complete days of organized practice."

Therefore supervised or organized conditioning exercises prior to the opening date for practice would be considered a violation of the 1965-1966 rules of the Minnesota State High School League, and in apparent conflict¹ with the recommendations of the National Federation of State High School Associations, of which Minnesota is a member.

Preseason Program of Exercises

Addressing itself to this problem, the Committee on Sports Medicine of the Minnesota State Medical Association has formulated a program of exercises which is available to all high schools throughout the state. Thus, all the participants in competitive sports have an equal opportunity to undertake a program of preseason conditioning that will increase the level of physical fitness prior to the organized football practice in an effort to reduce the in-

^{*}Published under the direction of the Committee on Medical Aspects of Sports of the Minnesota State Medical Association.

Continued

cidence of such injuries as are frequent in the early part of the season. However, it should be emphasized that physical fitness is only one of the factors that reduces the number of football injuries. Other factors are good coaching, proper equipment, adequate officiating, and good condition of the playing field.

A Physical Educator.

A careful search of the medical literature, as well as the literature in the field of physical education, failed to reveal a simplified program of progressive exercises for high school students without the need for uniforms or equipment. In the program of exercises to be presented, it is highly desirable that a trained leader, preferably a physical educator, lead the group on a regular basis so as to give continuity to the program as well as to ensure that the participants gradually increase the intensity of the exercises.

The exercises to be described are designed to improve the cardiovascular function, to strengthen muscles of the trunk and extremities, and to increase the flexibility of the body and legs. It is understood that once organized practice has

begun, the coach will take over the program of exercises as part of the practice training.

Captain's Practice.

These exercises were presented to representatives of the Minnesota State High School League which went on record stating that this program should be strongly encouraged. At the present time students in some high schools do participate in an informal and unsupervised program of preseason exercises known as "captain's practice." These groups of boys meet regularly and perform group exercises under a chosen leader, who may be the team captain.

These exercises should be performed in the order they are presented. The leader should determine the amount of exercise, unless the number is stated with the exercise.

Running

To Develop Endurance and Speed.

1. Begin with a total distance of $\frac{1}{2}$ mile and gradually increase until one mile is run each day. (Suggested routine: first slow, easy *run* for two to three minutes; then sudden, fast *sprint* for 15 to 20 yards; finally a fast *walk* for 50 yards. Repeat the sequence: run, sprint, and walk for the total distance of $\frac{1}{2}$ to one mile. Practice sharp turns to each side while running.) The sprinting may be started quickly on a signal from the leader. The running



Figure 1



Figure 2

should be done up and down hills; some could be done on steps or stairs, as in the stadium.

2. Run backward at best speed for 15 to 20 yards, and then quickly run forward for the same distance. Repeat two or three times.
3. Hop for 25 yards on one foot and repeat with the other foot. Hold opposite knee high, keeping hands on hips. Repeat two or three times.

To Condition Ankles (Figure 1).

Place chalk lines 15 inches on either side of a center line. Run with the feet apart, placing feet on outer lines.

Standing

To Increase Flexibility of the Trunk.

Side Bender (Figure 2).

Cadence: Moderately slow.

Starting position: Stand with feet apart, hands clasped over head and arms straight.

Movement:

1. With the right knee straight, bend body sideward slowly and as far as possible to the right.
2. Return to starting position.
3. Repeat (1) to left.

Repeat 10 times for each side.

Trunk Twister (Figure 3).

Cadence: Moderately slow.

Starting position: Stand with feet apart, hands behind head and knees straight.

Movement:

1. With knees straight, bend body obliquely to left and bring right elbow toward left thigh.
2. Return to starting position.
3. With knees straight, bend body obliquely to right and bring left elbow toward right thigh.
4. Return to starting position.
5. With knees straight, bend forward as far as possible.
6. Return to starting position.
7. With knees straight, bend backward as far as possible.

Repeat each movement 10 times.



Figure 3

To Strengthen Legs and Improve Endurance.

Stationary Run (Figure 4).

Cadence: First slow, then fast, then slow.

Starting position: Stand erect, with arms at thrust and fists lightly clenched.

Movement:

1. Begin slowly and speed up somewhat, raising knees to the height of the hips.
2. Run for a while at full speed, raising knees forcibly, then slow down.

From $\frac{1}{2}$ to one minute should be spent on this exercise.

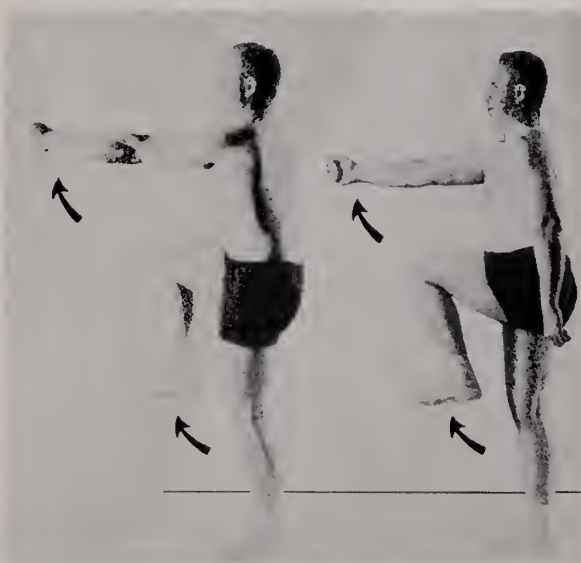


Figure 4

To Stretch Hamstring Muscles.

Hamstring Stretch (Figure 5).

Cadence: Moderate.

Starting position: Stand erect.

Movement:

Continued

1. Bend forward at the waist, with knees straight, and touch ground between feet.
2. Relax slightly and "bob" downward again, touching ground from 6 to 8 inches farther forward.
3. Repeat (2), touching ground still farther forward.
4. Return to starting position.

To Strengthen Upper Back Muscles and to Stretch Muscles of the Chest.

Shoulder-Blade Squeezer (Figure 6).

Cadence: Slow.

Starting position: Stand erect, with feet together and arms forward and level with shoulders.

Movement:

1. Swing arms sideward and backward as far as possible.
2. Relax slightly and swing arms backward again.
3. Repeat (2).
4. Return to starting position.

To Strengthen Muscles of the Neck.

Neck Firm (Figure 7).

Cadence: Moderate-to-slow.

Starting position: Stand erect, with fingers laced behind head.

Movement: (isometric)

1. Keeping elbows back, raise chest high,

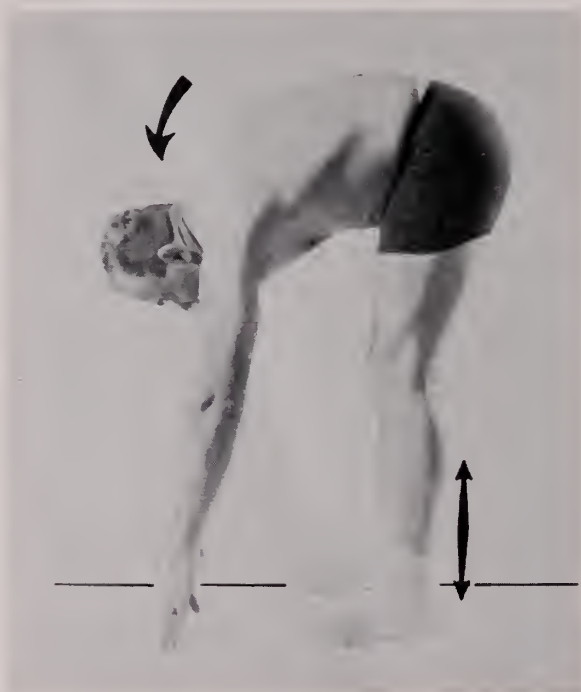


Figure 5



Figure 6

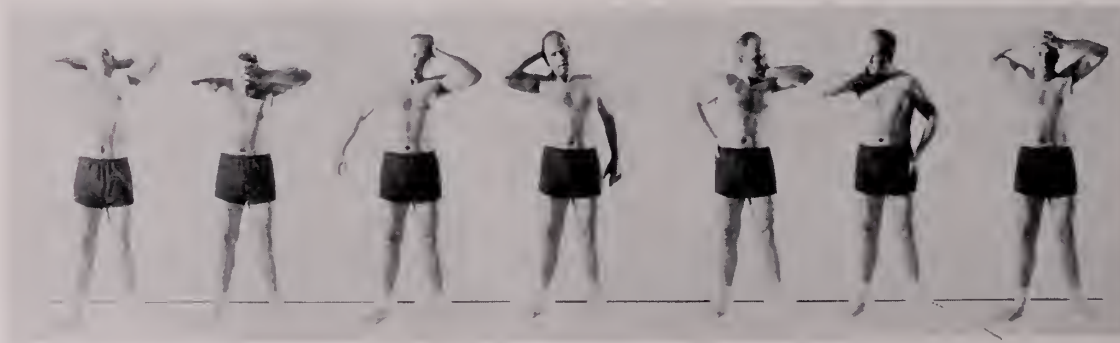


Figure 7

PRESEASON CONDITIONING EXERCISES

pulling head backward against resistance of hands. Repeat five times.

2. With fingers laced and held against forehead, push head forward against resistance. Repeat five times.
3. Hold left hand against left side of head. Attempt to touch ear to left shoulder, resisting motion with left hand. Repeat five times.
4. Reverse (3) to right side. Repeat five times.
5. Rotation. Place right hand on right side of lower jaw. Attempt to turn head to the right against resistance. Repeat five times.
6. Rotation. Reverse of (5). Repeat five times.
7. Circumduction. Tense all muscles of neck and move head in complete range of movement, first in clockwise motion and then counter-clockwise. Repeat five times in each direction.

Sitting

To Strengthen Abdominal Muscles.

Abdominal Strengthening—Sit-up (Figure 8).

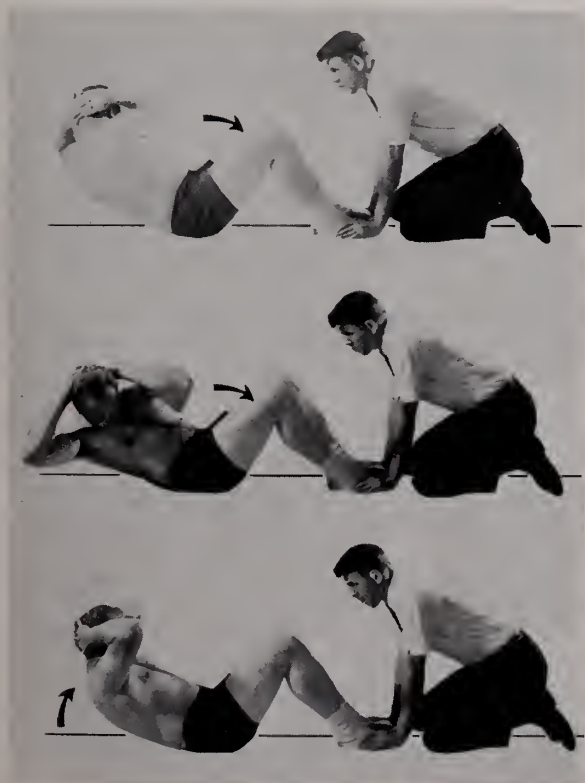


Figure 8

Cadence: Moderate.

Starting position: Lie on back, with knees bent and hands behind neck, feet held flat on ground by a teammate.

Movement:

1. Come to sitting position by "curling" the trunk, touching right elbow to left knee.
2. Relax slowly to recumbent position.
3. Repeat, touching right elbow to left knee first and then left elbow to right knee.
4. Come to sitting position, bringing head to between the flexed knees.

Repeat 10 to 30 times.

To Stretch Back and Hamstrings.

Hamstring Stretch (Figure 9).

Cadence: Moderate.

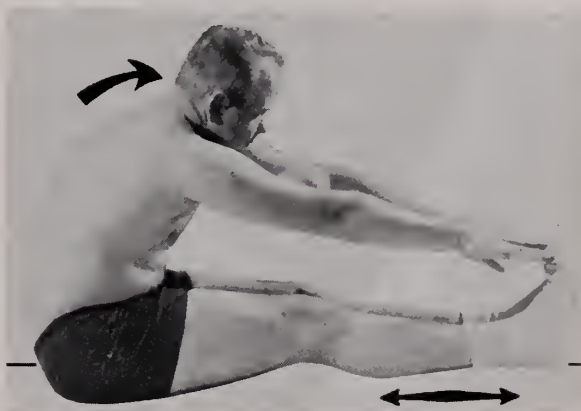


Figure 9

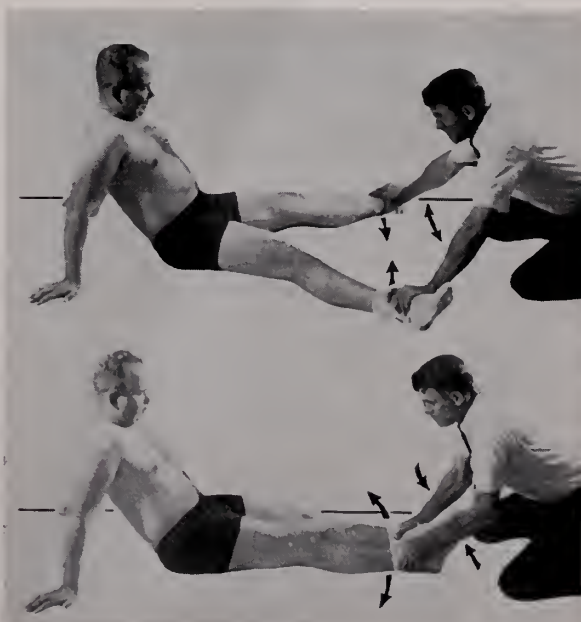


Figure 10

Starting position: Sit with knees straight.

Movement:

1. Bend forward and touch toes or grasp ankles while pulling trunk forward as far as possible.
2. "Bounce" downward three times.
3. Return to starting position.

Repeat five to 10 times.

To Strengthen the Muscles of the Groin.

Groin Strengthening (Figure 10).

Cadence: Moderate.

Starting position: Sit with legs outstretched and hands at side or in back of trunk for support, legs grasped at the ankles and held firmly by a teammate.

Movement: (isometric)

1. Move the legs against resistance of the teammate in strong efforts to bring the feet together.
2. Repeat above, except move legs apart against resistance.

Lying On Back (Supine Position)

To Increase Flexibility of the Trunk and to Strengthen Muscles of the Upper Back.

Leg-Back Stretch (Figure 11).

Cadence: Moderate.

Starting position: Lie flat on back, with arms outstretched at right angles to the trunk and palms flat on ground.

Movement:

With knees stiff and without moving shoulders, raise one leg to perpendicular position and swing it across the body until foot touches opposite hand.

Repeat 10 to 15 times for each leg.

To Strengthen the Muscles of the Legs and Trunk.

Bicycle (Figure 12).

Cadence: Moderate.

Starting position: Support body on shoulders, with elbows on ground and hands on hips.

Movement:

Raise legs and body as high as necessary in order to move feet and legs as rapidly as possible in an alternate motion, as in riding a bicycle.

Repeat 20 to 30 times.

To Strengthen Legs and Abdominal Muscles.

Leg Raiser-Straight Leg Raising (Figure 13).

Cadence: Moderate.



Figure 11



Figure 12



Figure 13

PRESEASON CONDITIONING EXERCISES

Starting position: Lie on back with feet together and arms at side of body.

Movement:

1. Raise left leg upward to the vertical.
2. With knees straight, lower left leg and at the same time raise right leg to the vertical.

Repeat 20 to 30 times.

To Strengthen the Muscles of Neck and Back.

Wrestler's Bridge (Figure 14).

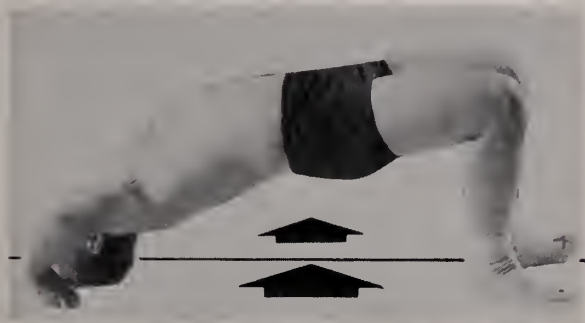


Figure 14



Figure 15



Figure 16

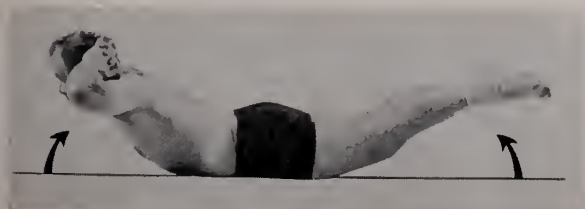


Figure 17

Cadence: Moderate-to-slow.

Starting position: Lie on back, with feet drawn up about a foot below hips, knees bent slightly farther than a right angle, fists clenched and placed by side of head, elbows forward.

Movement:

1. Raise the body as high as possible, resting the weight on fists, head, and feet.
2. Recover to starting position.

Repeat three to five times.

To Strengthen Muscles of the Hips.

Leg-Side Raiser (Figure 15).

Cadence: Moderate.

Starting position: Lie full length on right side, with head resting on outstretched right arm.

Movement:

1. Raise left leg as high as possible, keeping knee straight and leg in line with the body.
2. Repeat on left side, raising right leg as high as possible.

Repeat 20 to 30 times on each side.

Lying On Abdomen (Prone Position)

To Strengthen Muscles of Arms.

Push-up (Figure 16).

Cadence: Moderate.

Starting position: Rest with hands on ground on either side of chest, knees and hips straight.

Movement:

1. Bend elbows and touch chest to ground, keeping body straight.
2. Straighten elbows, raising body to straight line.

Repeat 10 to 20 times.

To Strengthen Muscles of Back and Neck.

Back Strengthening (Figure 17).

Cadence: Moderate.

Starting position: Lie on stomach, with hands behind head.

Movement:

1. With knees straight, arch back, lifting feet, legs, head, and chest off ground.
2. Repeat with arms extended fully over head.

Do each exercise 10 to 20 times.

Continued

To Strengthen the Muscles of the Extremities.

All Fours (Figure 18).

Cadence: Moderate.

Starting position: Lie with weight on hands and feet.

Movement:

Walk forward, backward, and sideward on hands and feet.

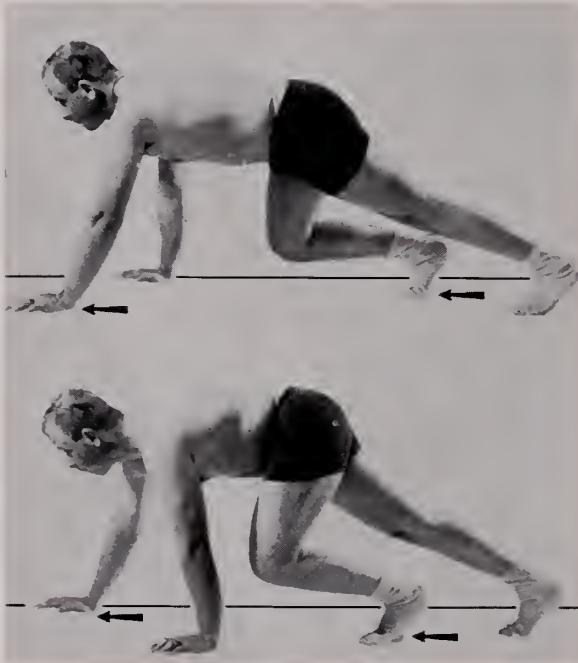


Figure 18

To Strengthen the Muscles of the Trunk and Extremities.

Elbow Extension Press-up (Figure 19).

Cadence: Moderate.

Starting position: Lie face down with legs straight out and hands clasped behind head.

Movement:

Resting on toes and elbows, lift all other parts of the body up away from the ground. Hold for count of three.

Repeat three to five times slowly.

Hand Extension Press-up

(alternative to Elbow Extension Press-up).

Cadence: Moderate.

Starting position: Lie face down with legs straight out and arms straight out as far as possible above head.

Movement:

Keeping elbows straight, press up on toes and hands. (This can be made into a competition by seeing how long each in-

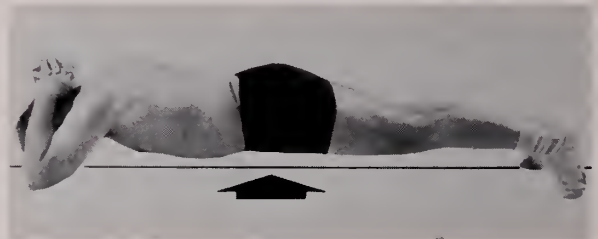


Figure 19



Figure 20



Figure 21

PRESEASON CONDITIONING EXERCISES

dividual can hold the position, with waist-line six inches from the ground.)

To Strengthen the Muscles of the Arms and Legs.

One-Hand Spider Drill (Figure 20).

Cadence: Moderate.

Starting position: Sit on right thigh, with legs outstretched, trunk leaning backward and weight resting on right arm.

Movement:

1. Straighten body to side-leaning rest position by raising hips and thighs as high as possible.
2. Walk in side-leaning position in a complete circle with the hand as the center of the circle of movement.

3. Repeat (2) but use opposite hand for support and walk in side-leaning position in opposite direction.

Repeat each exercise several times.

To Condition Chest.

Bouncer (Figure 21).

Cadence: Moderate.

Starting position: Lie flat on abdomen, with hands on ground.

Movement:

Start a push-up; quickly whip arms out to sides while dropping body to ground. Head should be back or turned to either side for the drop.

Repeat 10 to 20 times.

References

1. Honet, J. C., Fowler, W. S., Elkins, E. C., and Baker, C. E.: Effects of Training and Athletic Participation on Physical Performance of High School Boys. *Arch Phys Med* 43:51, 1962.
2. Knehr, C. H., Dill, D. B., and Neufeld, W.: Training and Its Effects on Man at Rest and at Work. *Amer J Physiol* 136:148, 1942.
3. The Forty-third Annual Official Handbook. Minnesota State High School League, 375 pp, 1965-1966.

It's the Law

Surgeon Physically Unable To Practice Specialty Is Totally Disabled

An insured physician, whose practice had been exclusively surgical, but who no longer could engage in such practice because of dermatitis on his hands, was entitled to benefits for total disability even though he was employed.

This physician was able to demonstrate to the court that, in the 10 years prior to his disability, his practice had been entirely surgical. Dermatitis developed on his hands, and despite continuous treatment, the dermatitis was not cured and flared up every time he scrubbed for surgery. The physician gave up his surgical practice and took a salaried position in a Veterans Administration Hospital.

The court ruled that, because of his inability to practice surgery, benefits were payable.

Case Reference—*Dixon v. Pacific Mutual Life Insurance Company*, 268 F.2d 812 (C.A. 2, June 19, 1959) The Citation Volume 15:5, June 15, 1967.

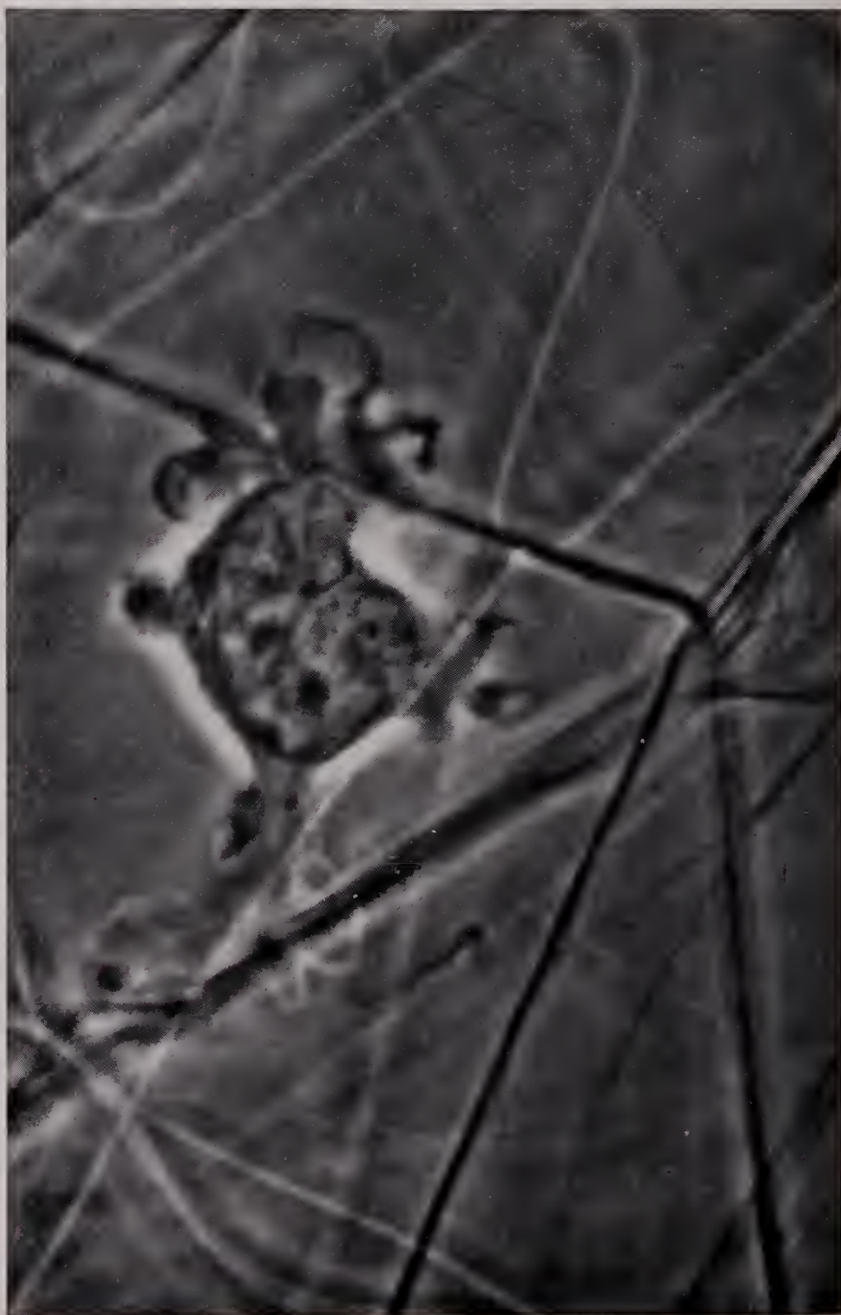
Duluth is the city so cooled by breezes wafted across Lake Superior that Mark Twain once remarked, "The coldest winter I ever spent was a summer in Duluth."
Saturday Review

INFLAMMATION: A cellular fight for life

A SYNTEX REPORT based on recently developed hypotheses about topical corticosteroids, including the cellular theories of inflammation by Thomas F. Dougherty, Ph.D., University of Utah.

You are looking at a fibroblast fighting for life. This cell—one of the most common found in connective tissue—has literally been poisoned by cytotoxins released from other cells that have ruptured. Soon, if the abnormal activity of this fibroblast does not cease, it, too, will rupture and die—one more casualty in the inflammatory wave of destruction precipitated by injury.

Until a short time ago no one had ever witnessed such a scene at the cellular level. Now, through advanced cinemicrographic techniques, it is possible to view and photograph the inflammatory process as produced experimentally in living animal tissue. This method permits new insight into the mechanism of inflammation and the role of corticosteroids in therapeutic management. Equally important, these techniques shed new light on factors that may make one corticosteroid more effective than another—factors that can be correlated with other chemical, biologic, and clinical parameters.

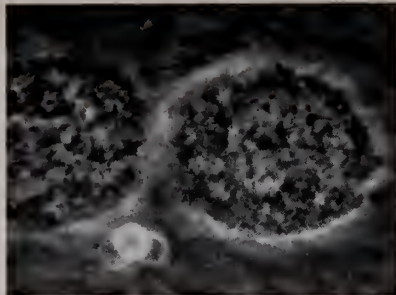


Visual evidence of how corticosteroids influence the inflammatory reaction

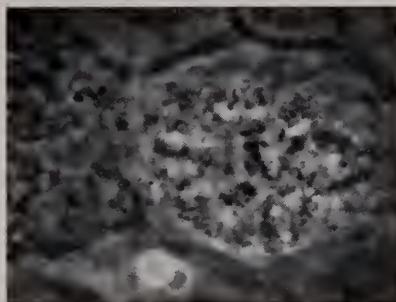
Working with phase-contrast cine-micrography on living animal tissue, Doctors Thomas F. Dougherty and David Berliner of the University of Utah College of Medicine have actually filmed cellular events that occur during the inflammatory reaction. This remarkable study* and additional work by these investigators, as well as by others, have established a new theoretical biologic basis for the antiinflammatory effect of the corticosteroids. (It must be noted that other theories, such as the lysosome or so-called "suicide bag" theory, have been postulated, although it is quite likely that there are more similarities than differences among the various theoretical models.)

The inflammatory wave of destruction

In this investigation an injurious injection of gelatin is used to set off an inflammatory reaction in living mouse tissue. What follows is a wave of destructive cellular activity that comprises the inflammatory response to injury. Mast cells (which contain heparin, serotonin and histamine) take up water, swell and rupture, releasing their contents, which are toxic outside the mast cell wall. These toxins, in turn, cause disintegration of other cells (such as fibroblasts) and the release of additional toxic material. Capillaries, too, take up water and leak unformed blood elements, causing edema. And polymorphonuclears, lymphocytes and perithelial cells invade the inflamed site. As a result of all these changes, the cellular environment reaches a state of turmoil.



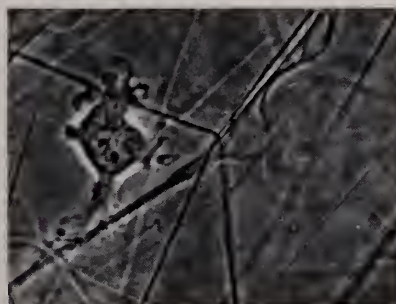
Phase-contrast microscopy showing mast cell before injury.



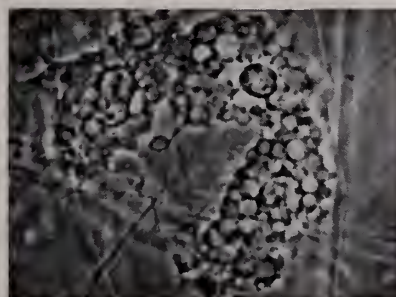
Mast cell (after injury) has broken up and released cytotoxins.

How corticosteroids change the picture

Corticosteroids appear to virtually stop the abnormal cellular activity that constitutes the inflammatory reaction. This permits the body's natural resources to clear up the inflamed area and repair the damaged tissue. This interpretation is supported by the fact that when the injurious gelatin solution is injected simultaneously with a corticosteroid — Synalar (fluocinolone acetonide) — the inflammatory pattern simply does not develop.



Fibroblast in high state of activity, much distorted.



Mast cells showing effects of corticosteroid action; cells are normal in size, shape and activity.

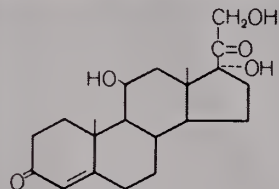


In summarizing his study Doctor Dougherty states: "...we also feel this work may explain why one corticosteroid helps a patient more rapidly and effectively than another. If it does, it is because one corticosteroid is the fastest, most effective inhibitor of the series of inflammatory events at the tissue level."

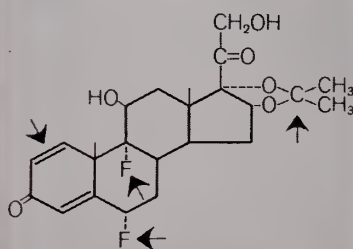
*A New View of Corticosteroid Action in Inflammatory Dermatoses, a film based on this study, is now available from your Syntex representative.

How advances in chemical design have achieved greater steroid potency

The chemical modification of corticosteroid molecules from the advent of hydrocortisone to the development of Synalar (fluocinolone acetonide) is a prime example of how biochemists can "design" to increase therapeutic activity and minimize undesirable side actions. Below, for example, we see the important changes that were made in reference to the hydrocortisone molecule to produce fluocinolone acetonide, one of the most active of all topical corticosteroids. As a result, a 0.01% preparation of Synalar (fluocinolone acetonide) has been reported to do the work of a 1% hydrocortisone product containing 100 times more corticosteroid. And it can often do it more effectively.



Hydrocortisone

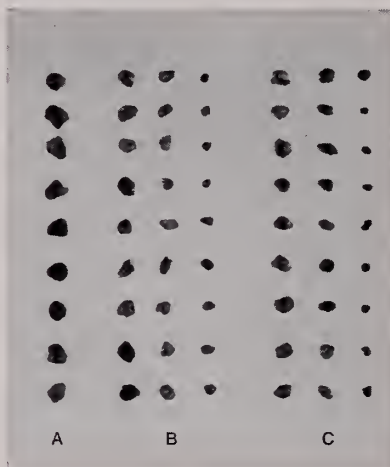


Fluocinolone Acetonide (Synalar)

- ☐ a double bond between carbons 1 and 2
- ☐ fluorine substitutions at both the 6- α , and the 9- α positions
- ☐ the addition of the acetonide at the 16- α , 17- α positions, thus providing one of the most potent topical corticosteroids available.

How bioassay tests are used to "predict" therapeutic potential

Biologic assays are another tool used by researchers to help establish the relative activity of corticosteroids. To date no single method of assaying corticosteroid activity has emerged as the ideal "yardstick" for predicting therapeutic potential. Taken together, however, these methods have proved useful. When such tests are run on various corticosteroids, a definite order of corticosteroid activity becomes evident. Compounds with the highest order of activity may be expected to merit clinical trial to establish their high therapeutic potential. When assayed by these methods, fluocinolone acetonide (Synalar) emerges as one of the most active topical corticosteroids, milligram for milligram, available for clinical application today.



THE THYMUS INVOLUTION ASSAY¹⁻⁴ is run on adrenalectomized rats. The sizes of the glands are measured, and the degree of involution caused by the steroid is determined as an indication of its potency. In the above photo, the comparative involution of thymus glands achieved with hydrocortisone and Synalar (fluocinolone acetonide) is shown. Untreated controls (A) show normal size. Group B— injected with 1, 2 and 4 mg. of hydrocortisone—show progressively smaller thymuses as does Group C— injected with fluocinolone acetonide—but with only 1/500th the dose of hydrocortisone.



THE ANTIGRANULOMA ASSAY¹⁻⁴ also utilizes adrenalectomized rats. Granulomas are induced by subcutaneous implantation of cotton pellets on either side of the thorax. The degree of granuloma inhibition achieved by a steroid reflects its potency. The above photo shows the inhibition of granuloma formation achieved with hydrocortisone and Synalar (fluocinolone acetonide). Untreated controls (A) show large, red granulomas adhering to the pellets. Group B, receiving hydrocortisone and Group C, receiving fluocinolone acetonide, show little, if any, granuloma formation. Fluocinolone acetonide produced the same effect as hydrocortisone with only 1/500th the dose. This assay, as well as the thymus involution assay, measures systemic rather than topical corticosteroid activity. Nevertheless, results by these methods correlate well with other assays and with the milligram potencies of topical steroids in current clinical use.

Worldwide clinical experience confirms the predictable therapeutic potential of Synalar

It is particularly gratifying that the promise of the advanced chemical design and high order of bioassay activity of Synalar (fluocinolone acetate) has been confirmed by widespread therapeutic application. Indeed, the impressive clinical response rate of Synalar has been documented in no fewer than 232 papers from 22 countries.

PRESCRIBING INFORMATION

For initiation of therapy: Cream 0.025%, 5 and 15 Gm. tubes, 425 Gm. jars; *for emollient effect:* Ointment 0.025%, 15 Gm. tubes; *for maintenance therapy:* Cream 0.01%, 15 and 45 Gm. tubes, 120 Gm. jars; *for intertriginous or hairy sites:* Solution 0.01%, 20 cc. and 60 cc. plastic squeeze bottles; *for infected inflammatory dermatoses:* Neo-Synalar® Cream (0.025% fluocinolone acetate, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes.

CONTRAINDICATIONS: Tuberculous, fungal, and most viral lesions of the skin, (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. **Contraindicated** in individuals with a history of hypersensitivity to any of the components. **PRECAUTIONS:** Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for pro-

Representative Clinical Results with Synalar*

Efficacy Documented in over 4,000 Patients

Condition	Number of *Publications	Number of Patients	Significant Improvement†
Contact Dermatitis	27	750	713
Eczematous Dermatitis	21	472	409
Seborrheic Dermatitis	18	442	426
Atopic Dermatitis	24	460	426
Psoriasis	36	1,699	1,510
Neurodermatitis	18	351	324
Total	144	4,174	3,808

*Complete bibliography on request.

†Expressed by the authors as excellent, very good, good, complete remission of inflammation, etc.

longed periods of time. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. When severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. **SIDE EFFECTS:** Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. The neomycin in Neo-Synalar Cream rarely produces allergic reactions.

REFERENCES: 1. Lerner, L. J., Bianchi, A., Turkheimer, A. R., Singer, F. M., and Borman, A.: Anti-inflammatory steroids: potency, duration and modification of activities. *Ann NY Acad Sci* 116:1071 (Aug. 27) 1964. 2. Idem: Comparison of anti-granuloma, thymolytic and glucocorticoid activities of anti-inflammatory steroids. *Proc Soc Exp Biol Med* 116:385 (June) 1964. 3. Ringler, A.: Activities of adrenocorticosteroids in experimental animals and man, in Dorfman, R. I.: *Methods of hormone research*, New York, Academic Press, 1964. vol. III. pp. 234-280. 4. Gubersky, V. R.: To be published.

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SYNTEX
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For inflammatory
dermatoses...
by any measure
a topical corticosteroid
of choice

Synalar® (fluocinolone acetate)

Milligram for milligram
one of the most active topical
corticosteroids available

Rapid and predictable
in antiinflammatory and
antipruritic activity

Results often comparable to
those of systemic corticosteroids
with fewer hazards

Sick, and worried sick



Professionally posed



Anxiety and tension stemming from organic illness may undermine your patient's cooperation and possibly retard success of primary therapy.

If his emotional symptoms persist in the face of your counsel and reassurance, you may want to consider adjunctive use of SERAX (oxazepam). It is indicated in anxiety, tension, agitation, irritability, and anxiety associated with depression. May be used in a broad range of patients, usually with considerable dosage flexibility.

When prescribing, carefully observe dosage recommendations and appropriate precautions, especially as pertaining to the elderly and when complications could ensue from a fall in blood pressure. (See Wyeth literature or PDR as well as "IN BRIEF" below.)

IN BRIEF.

Contraindications: History of previous hypersensitivity to oxazepam. Oxazepam is not indicated in psychoses.

Precautions: Hypotensive reactions are rare, but use with caution where complications could ensue from a fall in blood pressure, especially in the elderly. Withdrawal symptoms upon discontinuation have been noted in some patients exhibiting drug dependence through chronic overdose. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose; excessive, prolonged use in susceptible patients (alcoholics, ex-addicts, etc.) may result in dependence or habituation. Reduce dosage gradually after prolonged excessive dosage to avoid possible epileptiform seizures.

Withdrawal symptoms following abrupt discontinuance are similar to those seen with barbiturates. Caution patients against driving or operating machinery until absence of drowsiness or dizziness is ascertained. Warn patients of possible reduction in alcohol tolerance. Safety for use in pregnancy has not been established.

Not indicated in children under 6 years; absolute dosage for 6- to 12-year-olds not established.

Side Effects: Therapy-interrupting side effects are rare. Transient mild drowsiness is common initially; if persistent, reduce dosage. Dizziness, vertigo and headache have also occurred infrequently; syncope, rarely. Mild paradoxical reactions (excitement, stimulation of affect) are reported in psychiatric patients. Minor diffuse rashes (morbilliform, urticarial and maculopapular) are rare. Nausea, lethargy, edema, slurred speech, tremor and altered libido are rare and generally controllable by dosage reduction. Although rare, leucopenia and hepatic dysfunction including jaundice have been reported during therapy. Periodic blood counts and liver function tests are advised. Ataxia, reported rarely, does not appear related to dose or age. These side reactions, noted with related compounds, are not yet reported: paradoxical excitation with severe rage reactions, hallucinations, menstrual irregularities, change in EEG pattern, blood dyscrasias (including agranulocytosis), blurred vision, diplopia, incontinence, stupor, disorientation, fever and euphoria.

Availability: Capsules of 10, 15 and 30 mg. oxazepam.

To help you relieve anxiety and tension

Serax[®]
(oxazepam)



Wyeth Laboratories
Philadelphia, Pa.

Physician's Diary

While thou livest, keep a good tongue in thy head. — Shakespeare

Dr. A. B. Rosenfield, director of special services for the Minnesota Department of Health, was presented with the Community Service Award by the St. Paul Jaycees recently. Dr. Rosenfield received the award for his many years of outstanding dedication and leadership in the field of accident prevention and safety education.

* * *

Dr. L. J. Opsahl of Willmar has been appointed Kandiyohi County Coroner, and **Dr. William C. Bernstein**, St. Paul surgeon, was honored by the Mount Zion Temple Brotherhood with the presentation of its Eighteenth Annual Humanitarian Award. This award was presented to Dr. Bernstein for his contribution in the fields of education, civil rights, religion and medicine.

* * *

New Location: **Dr. John C. Mickelson** has left the Mankato Clinic to join **Dr. H. H. Edelbrock** in Los Angeles. . . . **Dr. S. A. Rahmaan** will practice in Buffalo Lake. . . . **Dr. James Terrain**, formerly of Thief River Falls, is to join the Klefstad Clinic in Greenbush. . . . **Dr. Gordon O. Greene** has left the Arlington Clinic to enter a three-year specialty program of study at the Mental Health Institute in Cherokee, Iowa. . . . **Dr. Gary R. Feigl** of Oxnard, California, has become associated with **Dr. E. C. Bayley** and **Dr. D. W. Sontag** in Lake City. . . . **Dr. Roland Larter** has taken up the practice of medicine in Karlstad. . . . **Dr. George Martin** will leave Karlstad to join **Dr. Peter Foderick** in Hallock. . . . **Dr. Norman Metcalf** will leave Princeton to take up a residency at the University of Minnesota School of Medicine.

* * *

Dr. James A. Cosgriff, Sr. was honored recently for his thirty-eight years of medical practice in the community of Olivia.

* * *

Bruce Gutzmann, former Shakopee veterinarian, recently served a two week preceptorship with **Doctor B. F. Pearson** in Shakopee. Mr. Gutzmann is presently studying medicine at the University of Saskatchewan, Saskatoon, Canada, and it is a requirement of the school to have all students studying to complete this two week training program.

* * *

Dr. John M. Vener, Arlington, has been elected to active membership in the American Academy of General Practice, and **Dr. Howard Wong** of Virginia has been certified as a Diplomate of the American Board of Obstetrics and Gynecology.

* * *

A pioneer center for diabetes detection and education has been established in Minneapolis through a three-year Community Health Services project grant. **Dr. Donnell**

D. Etzwiler of the St. Louis Park Medical Center will be the project's director.

* * *

Dr. Earl Elkins, a senior consultant in the Mayo Clinic's section of physical medicine, has been named Minnesota Physician of the Year. The honor was bestowed upon Dr. Elkins by Gov. Harold LeVander's Commission on Employment of the Handicapped at an awards luncheon.

* * *

Dr. Clark Millikan, senior consultant in a Mayo Clinic Section of Neurology, has been appointed chairman of the American Heart Association's Stroke Council.

* * *

Dr. Robert P. Buckley of Duluth was recently the guest speaker at the meeting of Range Medical Society. Dr. Buckley spoke on medical socio-economics.

* * *

Dr. E. A. Thayer, Fairmont physician, was recently the recipient of a WCCO Radio "Good Neighbor Award."

* * *

Doctors **Cameron G. Strong**, **Wiley M. Sams, Jr.**, **William P. Wharton**, **Carl Bernofsky**, **James Trautmann**, **Gerald A. Gronert**, **William W. Douglas** and **Jurgen Ludwig** have been appointed to the staff of the Mayo Clinic, Rochester.

* * *

Dr. Clarence J. Rowe, St. Paul, has been reappointed a member of the Committee on Mental Health in Industry of the American Medical Association.

* * *

J. C. Whitacre, II, M.D., has returned to Minneapolis after an absence of almost five years and opened an office for the practice of psychiatry in Minneapolis. During this period Dr. Whitacre studied in New York, Oklahoma and St. Louis completing his formal residency training at The Jewish Hospital of St. Louis, June 30 1967.

* * *

Newly elected members of the Minnesota Heart Association are: **Dr. John J. Juergens** of the Mayo Clinic, president; **Dr. James H. Kelly**, St. Cloud, president-elect; **E. William Quirin**, Rochester, second vice-president; **Dr. John Fee**, St. Paul, secretary; and **John L. Olson**, St. Paul, treasurer.

* * *

Doctors **Norman Goldstein**, **Alfred Uihlein** and **James Kernohan** of the Mayo Clinic were among the participants at the 21st National Convention of the American Trial Lawyers in Minneapolis during July.

Special Article

A Volunteer Physician in Vietnam

AFTER RECEIVING the assignment for Sixty Days in one of the provincial hospitals in Rach Gia, we were furnished with a round-trip, tourist-class airline ticket to Saigon. We were reimbursed at the rate of \$10.00 per day, a sum which adequately covered our living expenses.

The hospital was an old, one-story structure, built by the French with shutters to keep out the rain. The operating theater had been modernized by our government, and of the 350 beds, 100 were designated for use by our surgical unit.

Most of our work consisted of taking care of war casualties among the civilians and Vietnamese soldiers, though we also attended many Viet Cong members.

Cancer of the breast was usually far advanced; appendicitis was often found to be due to a ruptured appendix; and maternity problems were complicated because all normal deliveries were attended by midwives. Malaria was infrequent but parasitic disease was common, the *Ascaris* (roundworm) being often found within the peritoneal cavity when operating for bullet wounds.

We were pleasantly surprised at the recuperative powers of the Vietnamese people and their good response to antibiotics. Even though we often used large doses of chloromycetin, we observed no case of agranulocytosis or marrow depletion.

Most severe burns were caused by carelessness and the disregard for gasoline which the natives seemed to regard as similar to kerosene.



The city of Rach Gia has a population of 40,000 inhabitants. Curfew is at 9 P.M. when everybody gets off the streets, roads and rivers. After curfew the

Continued

saying goes: "The roads belong to the Viet Cong." Our little house, which for the sake of morale was called "Rach Gia-Hilton", is located on the river and adjacent to the hospital. Fishing boats line the river and in the background is the Gulf of Siam.



Here Dr. Pearson is treating a patient with Buerger's disease who has lost one foot and one hand but still refuses to give up his favorite brand of cigarettes which he pronounces "Saléme."



These four young women are midwives in the hospital. Watching them deliver babies, we found them to be very capable. All of them wish they could obtain a scholarship to America.

PHYSICIAN IN VIETNAM

The space between "Surgery" and "Emergency" is always filled with relatives and curious onlookers. The two girls in the foreground are native nurses.



Giving a prescription to natives is often done during the "Siesta" hour. These prescriptions can be filled at the hospital pharmacy or the Chinese pharmacy downtown. Workers insist on being paid not only for their own special holidays, but even for American holidays. Eighty per cent of the people are Buddhists.



Our house situated on the beach of Rach Gia River. Our group of doctors employed a cook and two servants.



Continued

Siesta hour is between 12:00 and 2:30, when everything stops, including the electricity, shutting off fans and refrigerators, and a large padlock must be placed on the Emergency Room so that if anyone arrives during the interval, it is "Syn Loi" (too bad). Here four American doctors are having their Siesta on the front lawn of their small house, on the banks of the river. In Vietnam rain comes twice daily and there is no shortage of water.



The birthrate is high and the infant mortality surprisingly low. Children appear well nourished; they live mostly on rice and fish.

Writing to my wife was usually done during the Siesta hour. In the background our private guard walks the river. There is no place in Vietnam which is one hundred percent secure; though Rach-Gia was considered to be only thirty-five percent secure, I felt in no danger. No American physician serving as a volunteer to these civilians has ever been harmed. I returned home with an increased respect and pride for our men in uniform and for the dedicated people who serve with the United States Agency for International Development. They live and work under frustrating and difficult conditions. Above all, I returned from this assignment with an increased appreciation of the amenities and advantages Americans enjoy and the privilege of being able

to come home to a great country like ours. I gained the impression that the majority of Vietnamese people, both North and South, would be eager to settle their differences on their own democratic terms, safely outside the dimensions of communist ideology. I found them all to be gracious, peace-loving citizens.

Bror Pearson, M.D.*
Shakopee, Minnesota

*Recently received the Certificate of Humanitarian Service under the American Medical Association Volunteer Physicians for Vietnam.



Remedies Derived From the Camel

A camel's brains, dried and taken in vinegar, are a cure, they say, for epilepsy: the same, too, with the gall, taken with honey; which is a remedy also for quinzey. A camel's tail dried, it is said, is productive of diarrhoea, and ashes of burnt camel's dung, mixed with oil, make the hair curl. These ashes, applied topically, are very useful for dysentery, as also taken in drink, the proper dose being a pinch in three fingers at a time; they are curative also of epilepsy. Camel's urine, it is said, is good for the cure of running sores.—Pliny

Law and Medicine

Therapeutic Abortion at the Mayo Clinic*

1945-1965

ALTHOUGH ETHICAL physicians find the act of abortion distasteful, occasionally circumstances exist in which the distaste for this procedure must yield to conscientious reason.

The legal profession has been attempting to clarify the authorization for abortion within certain limits. At present there is little variation in the laws regulating abortion in each state, and the fundamental principle of these laws is to preserve the life of the mother as well as that of her unborn child.¹⁰ In his interpretation of the law each physician is governed by his (1) medical knowledge, (2) medical ethics, (3) religion, and (4) degree of emotional involvement with his patient. However, the goal of both the legal and medical professions is to protect the well-being of the patient and, if possible, that of her offspring with the least possible risk.

Recently it has become evident that certain groups in the medical profession are seeking to liberalize the law as it pertains to therapeutic abortion. Legislation has been sought to approve abortion when (1) the physical or mental health of the mother is in danger, (2) the physical or mental health of the child is in danger, (3) the pregnancy has resulted from rape or incest, or (4) the pregnant patient is less than an arbitrary age, usually 15 or 16 years.

The desire to liberalize the law in this manner is thought-provoking, especially to obstetricians.

Pregnancies resulting from rape and incest and pregnancies in young girls can become medical or psychiatric problems. Frequently, however, the cause of these pregnancies is a social problem, not a medical one.

The present study is an appraisal of the indications for therapeutic abortion at the Mayo Clinic from 1945 to 1965. The purpose was to determine whether there have been changes in the medical or social indications for therapeutic abortion at this institution. A study was published in 1957 for the period from 1945 to 1955, and some data from that study have been incorporated in this paper.¹¹

Analysis of Cases

There has been a general decrease in the number of therapeutic abortions done during the second decade in comparison to the first decade (Table 1). The individual disease processes that necessitated therapeutic abortion fall into four major categories: (1) malignancy, (2) renal disease, (3) cardiovascular disease, and (4) neurologic disease—comprising 77% of the abortions done during the period of this study. Twenty-two per cent of the abortions were done for other medical reasons, and one abortion was done for socioeconomic reasons.

Although, in the strictest sense, destruction of a pregnancy during the treatment of carcinoma of the cervix cannot be considered a therapeutic abortion, this indication is included in the tabulation (Table 2). The largest number of abortions

Continued

*Read at the District VI meeting of the American College of Obstetricians and Gynecologists, Omaha, Nebraska, September 29 to October 1, 1966.

done were in patients who had carcinoma of the breast; eight of these 13 patients had metastatic disease.

Three of the five patients with brain tumors had malignancies that were incompletely removed. The remaining two patients were only suspected of having brain tumors. All five patients suffered from convulsive disorders.

TABLE 1
General Indications for Therapeutic Abortion at the Mayo Clinic

Indication	Number of Patients	
	1945-1954	1955-1964
Malignancy (all types)	18	11
Renal disease	19*	7**
Cardiovascular disease	9	2
Neurologic disease	8	3
Gastrointestinal disease	1	2
Diabetes mellitus	1	3
Psychiatric disease	2	1
Fetal indications	0	3
Miscellaneous	6	4
Total	64	36

*Eleven abortions because of toxemia.

**One abortion because of toxemia.

TABLE 2
Malignancy as an Indication for
Therapeutic Abortion at the Mayo Clinic

Malignancy	Number of patients	
	1945-1954	1955-1964
Cervix	3	1
Breast	8	5
Brain	1	4
Chondrosarcoma of hip	0	1
Spinal column	1	0
Hodgkin's disease	4	0
Leukemia	1	0
Total	18	11

TABLE 3
Renal Disease as an Indication
for Therapeutic Abortion at the Mayo Clinic

Renal diseases	Number of patients	
	1945-1954	1955-1964
Toxemia	11	1
Acute nephritis	0	1
Chronic glomerular nephritis (failure)	0	2
Chronic pyelonephritis	0	1
Infected hydronephrosis	0	1
Chronic renal insufficiency	3	1
Polycystic kidneys	3	0
Renal tuberculosis	2	0
Total	19	7

The need for radical surgery in the patient with chondrosarcoma of the right hip and the need for radiation therapy in the patients with lymphomas were the indications for abortion in the remaining five patients in this category.

In the group with renal disease, toxemia of pregnancy was the most common indication for therapeutic abortion (Table 3). This decreasing trend probably represents improved control, earlier treatment, and a better understanding of this disease.

The patients with congenital and rheumatic heart disease (Table 4) each had extremely low cardiac reserve. All four patients who underwent abortion because of chronic hypertension had severe retinal changes. The possibility of superimposed toxemia was the indication for interruption of pregnancy. The patient with pulmonary hypertension had suffered pulmonary embolism with infarction. Severe hypertension with low cardiac reserve was the indication for abortion in the patient with periarteritis nodosa.

The indications for abortion because of neurologic disease other than malignancy are listed in Table 5. Four of these abortions were carried out because of an exacerbation of multiple sclerosis or because the disease was far advanced. The patient with myasthenia gravis was a respiratory cripple who had undergone tracheotomy, and the woman with bilateral retinal detachment was considered to have retinal deterioration during the pregnancy. Each of the other patients listed had either progressive complications from her condition or marked residual handicaps.

Other conditions that required therapeutic abortions were numerous (Table 6). One patient with chronic ulcerative colitis had an acute exacerbation of the disease during the pregnancy, and another had secondary hepatic complications. The patient with duodenal ulcer had refractory symptoms complicated by hyperemesis.

All four patients with diabetes mellitus had retinal and renal complications.

One of the psychiatric indications for abortion was schizophrenia, and two abortions were done because of previous severe postpartum depression.

The patient with Raynaud's disease had suffered a sympathetic reflex dystrophy of the lower extremities after a previous pregnancy. The patient with Schoenlein-Henoch purpura had sec-

THERAPEUTIC ABORTION

ondary renal complications. The patient with osteomyelitis was to be in a spica cast for several months, and there was danger of postpartum infection. The patient with rheumatoid arthritis was severely deformed and had had previous exacerbations of her disease after each pregnancy.

Prior to 1949, four pregnancies were aborted because of pulmonary tuberculosis. No pregnancy has been terminated since that time because of this disease.

One patient underwent an abortion for socioeconomic reasons.

Three women had abortions because of fetal indications. Two women had had three stillbirths from erythroblastosis fetalis, and one had had rubella at three- to four-weeks' gestation.

One mother had an abortion because of the possibility of having a second child with fibrocystic disease.

Discussion

The number of patients and the variety of indications for therapeutic abortion make a comprehensive analysis of each indication impossible. Many of these patients had diseases that made continuation of pregnancy untenable. By the same token, a few of the indications for abortion were somewhat tenuous and certainly must be considered as being relative ones.

Medical research and increased therapeutic skill have changed the prognosis of many diseases. Consequently, pulmonary tuberculosis, toxemia of pregnancy, hyperemesis gravidarum, hypertension, infectious nephropathy, thyrotoxicosis, diabetes mellitus, and rheumatic fever only rarely dictate the need for abortion at the present time.^{3,6,9}

Malignancy

When viewing the broad category of malignancy as an indication for abortion, the physician must first consider the disease and then the pregnancy. If the pregnancy restricts tumor treatment, influences tumor growth, or is responsible for progressive complications, abortion may be indicated.^{6,11} Frequently, pregnancy causes increased edema and vascularity of brain tumors, with a worsening of seizure activity. Some breast malignancies appear to be estrogen dependent,

and occasionally the mother may gain some months of life by termination of the pregnancy. Also, some women with rapidly progressive inflammatory breast carcinoma probably should not become pregnant.

TABLE 4
Cardiovascular Disease as an Indication
for Therapeutic Abortion at the Mayo Clinic

Disease	Number of patients	
	1945-1954	1955-1964
Pulmonary hypertension	0	1
Periarteritis nodosa	0	1
Rheumatic heart disease	3	0
Congenital heart disease	2	0
Hypertension	4	0
Total	9	2

TABLE 5
Neurologic Disease as an Indication
for Therapeutic Abortion at the Mayo Clinic

Disease	Number of patients	
	1945-1954	1955-1964
Multiple sclerosis	3	1
Myasthenia gravis	0	1
Bilateral retinal detachment	0	1
Traumatic paraplegia	1	0
Protruded disk	1	0
Encephalitis	1	0
Previous postpartum intracranial hemorrhage	1	0
Post poliomyelitis	1	0
Total	8	3

TABLE 6
Other Conditions as Indications for Therapeutic
Abortions at the Mayo Clinic

Indication	Number of Patients	
	1945-1954	1955-1964
Gastrointestinal		
Chronic ulcerative colitis	0	2
Hyperemesis with duodenal ulcer	1	0
Diabetes mellitus	1	3
Psychiatric		
Schizophrenia	0	1
History of postpartum depression	2	0
Raynaud's disease	0	1
Schoenlein-Henoch purpura	0	1
Osteomyelitis of right hip	0	1
Rheumatoid arthritis	1	0
History of fibrocystic disease	1	0
Socioeconomic	0	1
Pulmonary tuberculosis	4	0
Fetal		
Erythroblastosis (3 stillbirths)	0	2
Rubella	0	1
Total	10	13

Continued

When a patient can be expected to live with the malignancy to the completion of pregnancy or when the pregnancy does not interfere with treatment, there seems to be little indication for interruption of that pregnancy. Such is the case with carcinoma of the vulva, carcinoma in situ of the cervix, and carcinoma of the colon.

Renal Disease

Chronic renal insufficiency, whatever the cause, may be an indication for therapeutic abortion. If renal failure ensues, the use of the artificial kidney or the consideration for renal transplant should not be hampered by the possibility of superimposed toxemia or obstructive processes caused by an enlarging uterus. Rarely, a similar situation can occur in patients with renal lithiasis or resistant infection of the urinary tract, especially in a patient with a solitary kidney.^{8,9,11}

Cardiovascular Disease

The increasing scope of cardiac surgery has completely altered the indications for therapeutic abortion in congenital and acquired heart disease.^{8,9,11} Few cardiac surgeons hesitate to operate on the pregnant patient at the present time, except in cases requiring prolonged and intensive anticoagulant therapy such as artificial valve implantation. Surgical procedures for coarctation and replacement of aneurysmal dilations are not contraindications to pregnancy. Cerebral aneurysms may rupture and cause acute episodes. These conditions are not necessarily improved by abortion of a pregnancy. With present modes of therapy, hypertension is only rarely uncontrollable.⁶

Fetal Indications

There are few absolute fetal indications for therapeutic abortion. Reports on the incidence

*Mayo Clinic and Mayo Foundation: Section of Obstetrics and Gynecology.

of congenital anomalies after rubella or other viral infections in the first weeks of pregnancy are inconsistent.^{7,12} At present, wholesale therapeutic abortion for these conditions does not seem valid.

The prognosis in erythroblastosis fetalis has been altered by exchange transfusion and recently by intrauterine transfusion. Immunologic studies may further decrease the necessity of therapeutic abortion for this condition.

Comment

Our list of indications for therapeutic abortion is not intended to be all-inclusive, and is meant only to emphasize that the indications are relative. Each complicated pregnancy must be evaluated for therapeutic abortion on its own merits. Abortion is not an innocuous procedure, and, under the best controlled conditions, complications and even death can occur.^{1,2,4,8} Psychic trauma and prolonged guilt reactions in the patient are not the least of these complications.^{4,8} Likewise, compounding the risk is not justifiable. Where therapeutic abortion is performed because of a chronic medical condition, sterilization should be done at the same time.^{5,8}

Conclusions

Clarification of the legal interpretation for therapeutic abortion is different from broadening the base for therapeutic abortion. This analysis of the 100 therapeutic abortions indicates that medical progress has markedly altered some of the indications for therapeutic abortions. However, it does not show that there has been a change in the attitude at this institution toward the relative indications for therapeutic abortion.

Richard S. Sheldon, M.D.*

David G. Decker, M.D.*

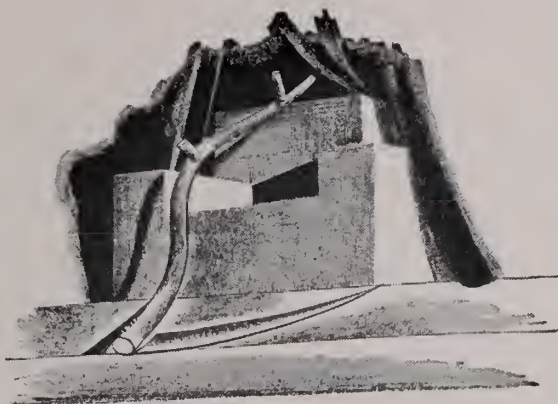
Rochester, Minnesota

References

- Berthelsen, H. G., and Østergaard, Erling: Techniques and Complications in Therapeutic Abortion. Danish Med Bull 6:105, 1959.
- Berthelsen, H. G., and Østergaard, Erling: Lethality and Incidence of Complications in Therapeutic Abortion in Denmark, 1953-1957. Danish Med Bull 6:110, 1959.

3-12 may be secured from the author or the reprints.

'Tis healthy to be sick sometimes.—Thoreau



In Memoriam

*I hear a voice you cannot hear,
Which says, I must not stay;
I see a hand you cannot see,
Which beckons me away.*

—Tickell

ALFRED T. KAPSNER, M.D.

Dr. Alfred T. Kapsner, 54, Princeton physician, died June 2. Born in Pierz, Dr. Kapsner graduated from the University of Minnesota Medical School, and had practiced medicine in Princeton since 1946.

He was a member of the East Central Medical Society, the American Medical Association, the Minnesota State Medical Association, and active in community activities.

Dr. Kapsner is survived by his wife, four sons and one daughter.

GEORGE R. McNEAR, JR., M.D.

Dr. George McNear, Jr., 44, Heron Lake physician, died May 27 at his home. Born in Boston, Massachusetts, Dr. McNear received his Doctor of Medicine degree at the Cornell University Medical School.

He was a member of the Windom Masonic Lodge, Prudence No. 97, A.F.&A.M., American Legion Post 224, the American Medical Association, the Academy of General Practice, the American College of Obstetricians and Gynecologists, the Minnesota State Medical Association and the Southwestern Minnesota Medical Society. He was an honorary Fellow of the Royal Society of Medicine, London, and the Royal College of Obstetrics and Gynecologists.

He is survived by his wife and two sons.

Disease as Reprisal I

*What sin did Miriam commit that she should be smitten with leprosy?
She had incensed the Lord by presuming to criticize Moses for having married
an Ethiopian woman and for being one of God's favorites.*

*And the Lord came down in the pillar of the cloud, and stood in the door of the
tabernacle, and called Aaron and Miriam: and they both came forth.*

*And the cloud departed from off the tabernacle; and, behold, Miriam became
leprous, white as snow: and Aaron looked upon Miriam, and, behold, she was
leprous. (Numbers 12: 5, 10.)*



"You're up ten pounds since your last physical. We're going to have to do something about that."

Get them while they're easily reversible.

Obesity doesn't happen suddenly. This insidious process has its beginning—and the chances of reversing it are better—during the *first 10 to 15 pounds of weight gain*.

When a new dietary pattern must be established, consider the adjunctive use of **BAMADEX SEQUELS**. Combining the proven *anorexigenic* action of d-amphetamine with the *tranquilizing* effect of meprobamate, **BAMADEX SEQUELS** controls appetite throughout the day, usually with a single capsule daily.

Contraindications: Dextro-amphetamine sulfate: In hyperexcitability and in agitated prepsychotic states. Previous allergic or idiosyncratic reactions to meprobamate.

Precautions: Use with caution in patients hypersensitive to sympathomimetic compounds, who have coronary or cardiovascular disease, or are severely hypertensive.

Dextro-amphetamine sulfate: Excessive use by unstable individuals may result in psychological dependence.

Meprobamate: Careful supervision of dose and amounts prescribed is advised, especially for patients with known propensity for taking excessive quantities of drugs. Excessive and prolonged use in susceptible persons, e.g. alcoholics, former addicts, and other severe psychoneurotics, has been reported to result in dependence on the drug. Where excessive dosage has continued for weeks or months, reduce dosage gradually. Sudden withdrawal may precipitate recurrence of preexisting symptoms such as anxiety, anorexia, or insomnia; or withdrawal reactions such as vomiting, ataxia, tremors, muscle twitching and, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, reduce dosage and avoid operation of motor vehicles, machinery or other activity requiring alertness. Effects of excessive alcohol consumption may be increased by meprobamate. Appropriate caution is recommended with patients prone to excessive drinking. In patients prone to both petit and grand mal epilepsy meprobamate may precipitate grand mal attacks. Prescribe cautiously and in small quantities to patients

with suicidal tendencies.

Side Effects: Overstimulation of the central nervous system, jitteriness and insomnia or drowsiness. Dextro-amphetamine sulfate: Insomnia, excitability, and increased motor activity are common and ordinarily mild side effects. Confusion, anxiety, aggressiveness, increased libido, and hallucinations have also been observed, especially in mentally ill patients. Rebound fatigue and depression may follow central stimulation. Other effects may include dry mouth, anorexia, nausea, vomiting, diarrhea, and increased cardiovascular reactivity.

Meprobamate: Drowsiness may occur and can be associated with ataxia; the symptom can usually be controlled by decreasing the dose, or by concomitant administration of central stimulants. Allergic or idiosyncratic reactions: maculopapular rash, acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever, transient leukopenia. A case of fatal bullous dermatitis, following administration of meprobamate and prednisolone, has been reported. Hypersensitivity has produced fever, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis (1 case), anaphylaxis, agranulocytosis and thrombocytopenic purpura, and a fatal instance of aplastic anemia, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity, usually after excessive dosage. Impairment of visual accommodation. Massive overdosage may produce drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Bamadex[®] Sequels[®]

Dextro-amphetamine sulfate (15 mg.)
with Meprobamate (300 mg.)

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466-7

**Os
frontale**

**Sinus
frontalis**

**Crista
galli**

**Os
nasale**

Lamina cribrosa ossis ethmoidalis

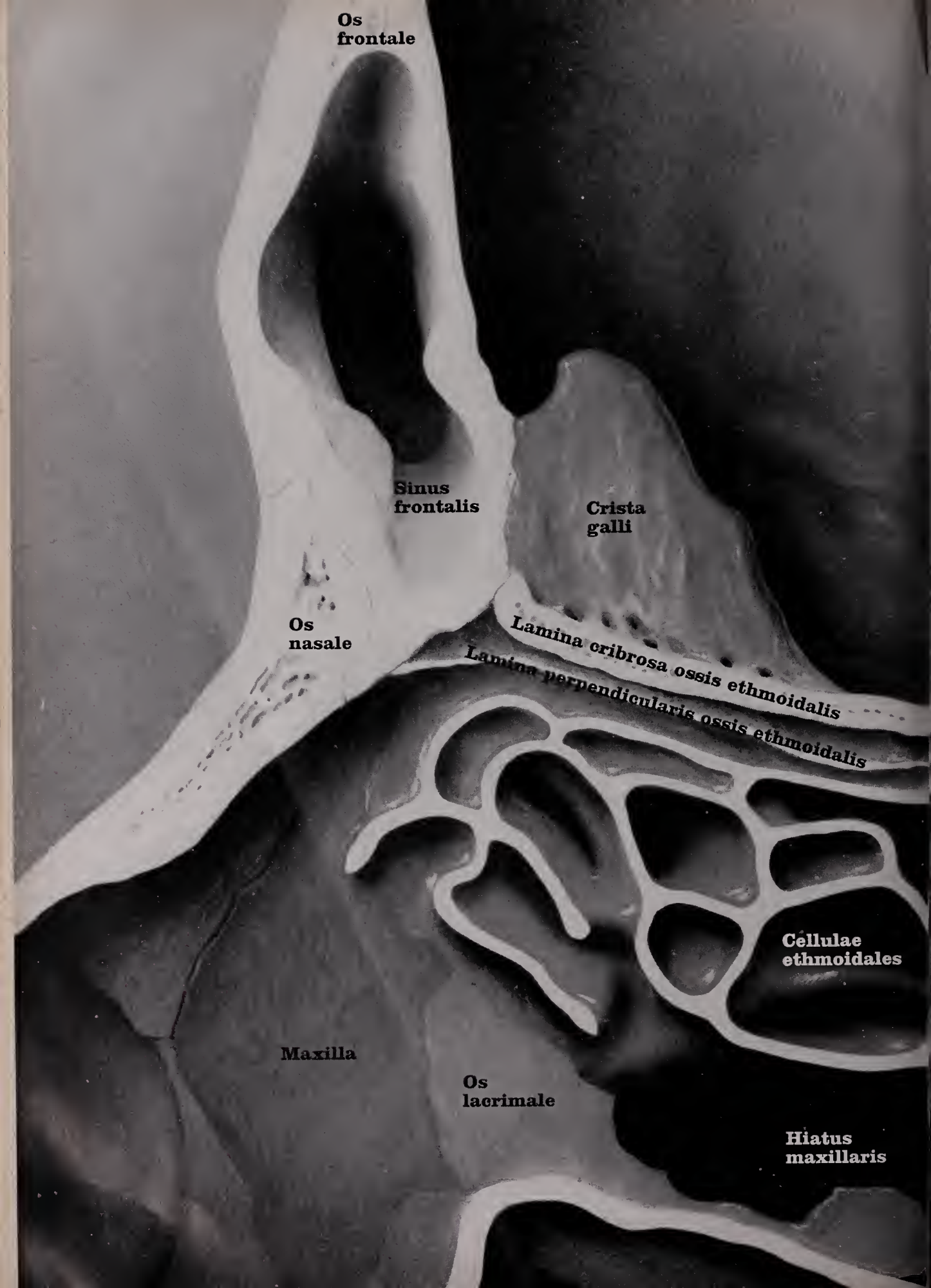
Lamina perpendicularis ossis ethmoidalis

**Cellulae
ethmoidales**

Maxilla

**Os
lacrimal**

**Hiatus
maxillaris**



special formula for a special problem

*specifically formulated
for symptomatic
relief of sinus headache*

Sinus headache is not a single entity,
but a chain reaction of pain.
It is facial pain—deep, dull, aching and
nonpulsating. It is referred pain—
originating in the nose and sinuses but
felt at another site. It may become
generalized pain and tension in head and
neck. It is one or all of these.

The Sinutab formula is designed
for symptomatic relief of sinus headache.

It provides two analgesics to relieve
pain and discomfort...an effective oral
decongestant to reduce mucosal congestion...
and an antihistamine to help
control allergic manifestations.

Side Effects: Epigastric distress, drowsi-
ness, dizziness, insomnia and nervousness.

Precautions: Instruct patients not to drive
or operate machinery if drowsiness occurs.

Use with caution in patients with thyroid
disease, heart disease, hypertension, diabetes
or kidney disease. Excessive dosage or
prolonged use may cause kidney damage.

Dosage: Adults—2 tablets every 4 hours.

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SINUTAB[®] for sinus headache

Each tablet contains
150 mg. acetaminophen,
150 mg. phenacetin,
25 mg. phenylpropanolamine HCl,
and 22 mg. phenyltoloxamine
citrate.

E-OP-71-CC



**Sinus
sphenoidalis**

**Os
occipitale**

Public Health Nursing

Guide for Agencies in Developing Written Medical Policies for Public Health Nursing Services*

MEDICAL AND nursing policies serve as a guide for general nursing practice and are essential for the assurance of quality services to patients. Medical policies also promote good professional relationships between the practicing physicians and the (name of agency) nursing staff.

This guide for medical policies has been jointly agreed upon by the Public Health Nursing Committee of the Minnesota State Medical Association and the Section of Nursing, Minnesota Department of Health. The guide is intended to be useful to local public health nursing committees, nurses and physicians in developing their own medical policies. Such policies should apply to local situations and should have the official approval of the Agency's Medical Advisory Committee.

A public health nursing program for any community includes:

1. Part-time or intermittent home nursing care for the physically or mentally ill and disabled.
2. Health counseling.
3. Participation in community measures to prevent disease and to establish needed health services.

In addition to home nursing care services, the public health nurse offers health guidance to the entire family. She serves families through the home, school, at work and in clinics. She has contacts with many persons who are not ill but who might benefit by health instruction and health guidance.

When a community provides public health nursing services, they are available to everyone, rich or poor, and without regard to race, color or creed.

Medical Advisory Committee

It is essential to establish a medical advisory committee to consider and recommend medical policies and standing orders necessary in a pro-

gram of nursing care of the sick at home. In the appointment of such a committee, general practitioners and medical specialists should be considered. Three to five physicians—one of whom should be the physician on the administrative body (County Nursing Committee)—usually compose this group.

Functions of the Medical Advisory Committee

1. Recommend and approve policies regarding the medical aspects of the agency program.
2. Assist in interpretation of the nursing care services to other physicians and persons in the community.
3. Approve any publicity that involves medical information to be sent to physicians or used through public media.
4. Approve the content and frequency of health examinations for the employees of the public health nursing agency before and during employment and to advise regarding a health program for the staff.

The following suggested medical policies may be established by the agency with the approval of the Medical Advisory Committee.

Policies Related to Medical Supervision

Except under highly unusual circumstances, public health nurses are not expected to answer to the direction of persons other than licensed physicians and surgeons. They may, however, carry out nursing procedures under the orders of other licensed health practitioners when such orders are within the limits of the practitioner's licensure and compatible with the role of the public health nurse.

The patient's physician should be contacted when the care is requested by the patient, his family, or others.

Out-of-Town Physicians: If a patient, visiting temporarily in the community, requests treatment

Continued

*Revision of "Guide" published Minnesota Med. February, 1962.

ordered by his home physician, from whom he has written orders, the nurse may give treatment. If the patient remains in the community, the renewal of treatment orders should be secured in accordance with policies established herein.

For physically ill or disabled patients without medical supervision, usually only one visit is made before medical care is arranged. Standing orders approved by the medical advisory committee are to be followed on this visit. Medical supervision is to be advised and available resources for medical care explained. If a *second* or *third* visit is necessary to arrange for medical care, the essential nursing care is to be given but the importance of calling a physician should be re-emphasized. If needed, help is given in obtaining these services. Persons unable to pay for private medical care are to be referred by the nurses to the responsible community agency.

Selection of Physician—If a patient is not under medical care and wishes recommendations concerning securing a private physician, the nurse may advise the family to call the local medical society, the hospital or in a small community the nurse, who may give the family the names of the physicians. The family should then make its own selection.

In an emergency where the family or the family physician cannot be reached, public health nurses should call the medical representative on the nursing committee, a member of the medical advisory committee or the health officer.

Policies Related to Orders for Care

Telephone orders from the patient's physician may be accepted by a professional nurse member of the staff; however, these orders should be confirmed in writing within 48 hours.

Medical orders should be reconfirmed in writing at appropriate intervals and at least every two months. Special attention should be given to renewal of orders to administer hypodermics containing narcotics.

For continued nursing care in long term illness, the patient should be seen by the physician at least every six months.

Orders for medication must include the following information: diagnosis, name of drug, exact dosage of drug, and frequency, method, and site of administration.

Nurses are permitted to give intradermal and

subcutaneous and intramuscular injections on written orders from a physician. The nurse may *not* give intravenous injections, sera or drugs which commonly cause severe reactions. The physician on the nursing committee or a member of the medical advisory committee will be consulted about requests for injections of any questionable drugs.

With the written consent of the physician, a responsible family member or other person approved by the family may be taught to give a subcutaneous and intramuscular injection. (See Policies for Home Health Aide Services.*) Some agencies may wish to develop other policies such as catheterization of male patients.

Policies on Administration of Drugs

In the interest of patient safety, policies governing the administration of certain drugs by the public health nurse should be established.

The nurse should never administer a drug unless she knows the name of the drug and is familiar with its action. A medication bearing a prescription number only must be identified before it is administered. It is important for the nurse to be familiar with the medication she is administering and the reactions of the medication for the purpose of observing the patient intelligently.

Detailed policies for other medications may be desirable.

Guidelines for a Penicillin Policy follow:

Because of the serious problem of reaction to penicillin, the following precautions have been established for the safety of the patients and the protection of the nurses:

1. New patients should be questioned about any type of allergy in themselves or in their family. When assigned to a patient requiring penicillin, the nurse will carry an emergency adrenalin kit whenever she administers medication.

2. The first injection of each series of penicillin is to be administered by the physician. A series is defined as a regular sequence of doses continued for a definite period of time.

3. Further injections may be administered by the nurse on written order of the physician. Before giving each injection, the nurse is to question the patient for symptoms of allergic reaction.

4. It is recommended that the nurse organize her visit so that she will be in the home for 20-30 minutes after she has given the injection, because

*See Minnesota Med 45: 203, 1962.

a reaction may occur after any injection of penicillin.

5. Anaphylactic reaction may occur within 30 seconds after injection, beginning with itching of the eyes, feeling of fullness in the face, tingling of the extremities, tightness of the chest, and choking sensation, pallor, dyspnea, cyanosis, rapid development of shock and death. Nausea, vomiting, and diarrhea may also be present.

6. If anaphylactic reaction occurs in adults, give 0.5 cc. of adrenalin chloride, 1:1000 intramuscularly. WASTE NO TIME. Massage area for quick absorption. If symptoms are not relieved, a repeat dose of 0.5 cc. may be given in ten minutes. Have someone in the home notify the physician immediately while nurse is giving the adrenalin. If alone with the patient, give adrenalin first and then contact physician. Give external treatment for shock. Report the situation to the physician on the nursing committee as soon as convenient.

7. Dosage of adrenalin for children must be made on an individual basis. However, the following scale may be used as a safe guide:

Children under 5 years	0.1 cc
Children between 5-10 years	0.2 cc
Children over 10 years	0.2 cc-0.5 cc
increase proportionately	
according to weight—up to 0.5 cc	

If symptoms are not relieved, repeat only once in ten minutes.

8. Also report to the doctor all other milder reactions observed following a penicillin injection.

Suggested Standing Orders for Nursing Care

The purpose of standing orders is to provide directions for emergency nursing care until the patient's physician can be contacted. Standing orders are endorsed by the medical advisory committee.

Patient with Fever

Take and record TPR. Advise calling physician. Isolate, if communicable disease is suspected. Give sponge bath, if rectal temperature is 102.6° or higher. If abdominal pain is present, advise nothing by mouth until physician's orders are obtained. If there is no abdominal pain, fluids by mouth may be recommended. Boiled water should be given infants.

Conditions of the Eyes

Infants with discharging eyes:

Report immediately to the patient's physician.

Adults:

Foreign bodies in the eye—do not attempt to remove an embedded body. If foreign body is not embedded, carefully remove it with moistened cotton-tipped applicator. If it does not come out after two or three attempts, bandage eye securely but not tightly and refer to physician.

Other Eye Conditions:

Persons with inflamed or discharging eyes should be referred for immediate medical care. In all cases of discharging eyes, stress isolation of the patient.

Conditions of the Ears

Discharging ears:

Cleanse outer ear with cooled, boiled water and cotton. Dry thoroughly. Do not irrigate. Allow free drainage (do not use cotton ear-plugs). Apply lubricant to skin of ear to protect from discharge. Refer to physician.

Foreign body in ears:

Instill warm water if insect is suspected. Obtain medical care immediately. Artificial light may attract an insect.

Infant Diarrhea

Obtain immediate medical care. Stop all food and advise giving only boiled water. Keep buttocks and genitalia clean and dry. Urge careful hand washing by those giving infant care.

Upper Respiratory Infections Including Sore Throat and Earache

Advise medical care. Stress isolation and rest in bed. Take TPR. Encourage fluids and diet as tolerated. Instruct family to burn oral and nasal discharges.

Burns

Mild (skin unbroken, no blisters):

Hold burned part under cold running water for two or three minutes or apply ice.

Severe (all burns other than mild):

Obtain immediate medical care or send patient to hospital at once. Treat the patient for shock. Have him lie down with his head slight-

Continued

ly lowered. Cover him to avoid exposure.

Do not apply ointment.

Chemical:

1. Wash with large quantities of running water (except those caused by phosphorus).

2. Immediately after, cover with loosely applied clean cloth.

3. Avoid use of ointments, greases, powders, and other drugs in first-aid treatment of burns.

4. Treat shock by keeping patient flat, keeping him warm, and reassuring him until arrival of physician.

Dressings

Minor wounds:

Cleanse with soap and water; protect with clean, dry dressing; advise calling physician if indicated.

Major wounds:

Cover with sterile gauze and control bleeding by applying pressure dressings at site of injury. Obtain medical help immediately.

Surgical wounds:

If drainage or bleeding is excessive, call physician immediately. Reinforce dressing if necessary.

Convulsions

Infant and early childhood:

Protect from external injury such as falls and burns. Protect from biting tongue or allowing it to obstruct air passage. This can be done by putting a thick wad of cloth between the teeth, if possible. Keep air passage free from mucus and turn face to one side to prevent aspirating of saliva or vomitus. Obtain medical care. After convulsion subsides and if accompanied by high fever, give tepid water sponge bath continuously until fever is reduced.

Adult:

Protect from external injury and biting of tongue the same as with infants and children. Do not restrain patient. After attack is over, allow patient to sleep without disturbing or questioning him. Obtain medical care.

Poisons

Call a physician *immediately*. He may wish to make use of a regional Poison Information Center. Speed is essential to stop absorption of a poison. If possible, one person should begin first-aid while another calls a physician. The

nature of the poison will determine the first-aid measure to use. Save and give to the physician or hospital the poison container with its intact label and any remaining contents. If the poison is unknown, bring along the vomitus for examination. Do not induce vomiting if:

Patient is in a coma or unconscious

Patient is in convulsions

Patient has swallowed a petroleum product, e.g., kerosene, gasoline, lighter fluid

Patient has swallowed a corrosive poison (symptoms—severe pain, burning sensation in mouth and throat, vomiting)

Swallowed Poisons

Call a physician immediately if the patient has ingested a corrosive poison as:

1. Acid and acid-like corrosives; sodium acid sulfate (toilet bowl cleaners), acetic acid (glacial), sulfuric acid, nitric acid, oxalic acid, hydrofluoric acid (rust removers), iodine, silver nitrate (styptic pencil).

2. Alkali corrosives; sodium hydroxide—lye (drain cleaners), sodium carbonate (washing soda), ammonia water, sodium hypochlorite (household bleach); and

If the patient can swallow, give the following:

For acids: milk, water, or milk of magnesia (1 tablespoon to 1 cup of water)

For alkalis: milk, water, any fruit juice or vinegar

For patients 1-5 years old—1 to 2 cups

For patients 5 years and older—up to 1 quart
If patient has ingested a non-corrosive substance:

Give milk or water and induce vomiting by placing the blunt end of a spoon or your finger at the back of the patient's throat, or by use of this emetic—2 tablespoons of salt in a glass of warm water. When retching and vomiting begin, place patient face down with head lower than hips. This prevents vomitus from entering the lungs and causing further damage.

Inhaled Poisons

1. Carry patient (do not let him walk) to fresh air immediately.

2. Open all doors and windows.

3. Loosen all tight clothing.

4. Apply artificial respiration if breathing has stopped or is irregular.

Continued

5. Prevent chilling (wrap patient in blankets).
6. Keep patient as quiet as possible.
7. If patient is convulsing, keep him in bed in a semidark room; avoid jarring or noise.
8. Do not give alcohol in any form.

Skin Contamination

1. Drench skin with water (shower, hose, faucet).
2. Apply stream of water on skin while removing clothing.
3. Cleanse skin thoroughly with water; rapidity in washing is most important in reducing extent of injury.

Eye Contamination

1. Hold eyelids open, wash eyes thoroughly with gentle stream of running water immediately. Delay of few seconds greatly increases extent of injury.
2. Continue washing until physician arrives.
3. Do not use chemicals; they may increase extent of injury.

Injected Poisons (scorpion and snake bites)

1. Make patient lie down as soon as possible.
2. Do not give alcohol in any form.
3. Apply constricting bend above injection site (e.g., between arm or leg and heart). The pulse in vessels below the constricting bend should not disappear, nor should the constricting bend produce a throbbing sensation. The constricting bend should be loosened for 1 minute every 15 minutes.
4. Apply ice-pack to the site of the bite.
5. Carry patient to physician or hospital; *do not let him walk.*

Accidents—Control of Bleeding

The nurse will follow the accepted procedures described in the American Red Cross First Aid Handbook. Medical care should be arranged for immediately.

Other Standing Orders

Some agencies may wish to adopt other standing orders in relation to foot care for the diabetic and elderly; decubitus ulcers, impactions, etc.

References

1. Various materials from Department of Public Health Nursing, National League for Nursing.
2. "To Prevent Poisoning . . ." American Medical Association, May 1967.

Heberden's Syndrome

Precordial, substernal, epigastric, or occasionally jaw area pain which originates from spasm or partial atheromatous occlusion of one of the coronary arteries was described first by Heberden as angina pectoris in 1785.

The discomfort of angina pectoris varies from a mild sensation of weight or pressure felt after exertion or following meals to severe recurrent paroxysms, which may eventually appear while resting or sleeping. This latter type is particularly characteristic of preinfarction anginal syndrome. The pain of true angina pectoris may radiate to the anterior shoulder area, the inner aspect of the arm, the anterolateral portion of the neck, or just above the angle of the jaw. Long continued or severe attacks are often followed by coronary occlusion and myocardial infarction.

Angina pectoris should be differentiated from pseudoangina, anterior chest wall pain, and hiatus hernia. An electrocardiograph may give evidence of coronary disease; if not, a two-step exercise curve may be diagnostic. Immediate pain relief may usually be obtained by nitrites; however, if myocardial infarction supervenes, the value of nitrites is sharply limited. If severe angina pectoris is recurrent the prophylactic use of anticoagulants is indicated.

Durham, Robert H.—*Encyclopedia of Medical Syndromes*
Hoeber Medical Division, Harper and Row, New York



Meetings and Announcements

Most people would die sooner than think; in fact, they do so.—Bertrand Russel

AUGUST

American Academy of Physical Medicine & Rehabilitation, (E), Sherman House, Chicago, Aug. 17-22. Exec. Dir.: Creston C. Herold, 30 N. Michigan Ave., Chicago 60602.

International Biophysics Congress, Third, Boston, Mass., Aug. 29-Sept. 3. Info: Dr. Walter Rosenblith, Center of Communication Sciences, Room 20B-221, Massachusetts Institute of Technology, Cambridge 02139.

Wyoming State Medical Society, Jackson Lake Lodge, Moran, Aug. 26-29. Exec. Sec.: Arthur R. Abbey, P.O. Box 2266, Cheyenne 82001.

American Association of Electromyography and Electrodiagnosis, Americana Hotel, Miami Beach, Fla., Aug. 27. Info: M. K. Newman, M.D., 16861 Wyoming Ave., Detroit 48221.

American Dietetic Association (Golden Anniversary Meeting), Conrad Hilton Hotel, Chicago, Aug. 14-18. Exec. Sec.: Ruth M. Yakel, 620 N. Michigan Ave., Chicago 60611.

American Hospital Association, (E), Palmer House, Chicago, Aug. 21-24. Exec. Vice Pres.: Edwin L. Crosby, M.D., 840 N. Lake Shore Dr., Chicago 60611.

Black Hills Medical Seminar, Rapid City, S. D., Aug. 4-5. Chair.: Richard Kovarik, M.D., 728 Columbus St., Rapid City, S.D. 57701.

National Medical Association, Chase Park Plaza, St. Louis, Aug. 7-10. Adminis. Sec.: Samuel C. Smith, 520 W St., N.W., Washington, D. C. 20001.

Minnesota Academy of General Practice Meeting, August 24-27. Summer Retreat, Grand View Lodge, Brainerd, 8:00 A.M.-12:00 P.M.

SEPTEMBER

Annual convention Southern Minnesota Medical Association, Friday, September 15, Shuttuck Hall, Faribault. Contact: J. J. Eustermann, Program Chairman, Mankato Clinic, Mankato.

Association of Minnesota Internists Meeting, September—To be set

Scott-Carver County Medical Society Meeting, September 5, Wagner Supper Club, Jordon, Minnesota, 7:30 P.M.

Zumbro Valley Medical Society Annual Meeting, Plummer Hall, 8:00 P.M., September 6.

Minnesota-Dakota-Manitoba Orthopedic Society, Annual Meeting, Rochester, Minnesota, September 8-9 (Tentative).

Minnesota Radiological Society Annual Fall Meeting, Brainerd, Minnesota, September 9-10.

Southwestern Minnesota Medical Society Meeting, September 11, Ehlers Supper Club, 7:00 P.M.

St. Louis County Medical Society Executive Committee, St. Mary's Hospital, 6:00 P.M.—Regular Meeting, St. Mary's Hospital, 8:00 P.M., September 14.

Minnesota Academy of General Practice, AAGP Congress of Delegates, Dallas, Texas, September 16-18; AAGP Scientific Session, Dallas, Texas, September 18-23.

Hennepin County Academy of General Practice Membership Meeting, Minneapolis Athletic Club, 6:00 P.M. Social Hour; 7:00 P.M. Dinner; 8:00 P.M. Program, September 18.

Blue Earth Valley Medical Society Meeting, September 20, Interlaken Golf Club, Fairmont, 7:00 P.M.

McLeod County Medical Society Meeting, September 21.

Twin City Urologic Society Meeting, September 21, Town and Country Club, St. Paul, 6:00 P.M.

Northwestern Pediatric Society General Meeting, White Pine Inn, Bayport, 9:30 A.M. (All Day and Dinner), September 22.

Ramsey County Medical Society Regular Meeting, 1500 Lowry Medical Arts Building, St. Paul, 8:00 P.M., September 25.

Lyon-Lincoln County Medical Society Business Meeting, Chalet Club, Marshall, 6:30 P.M., September 26.

Range Medical Society Regular Meeting (Place not yet determined), 6:30 P.M., September 26.

Minnesota Chapter, American Academy of Pediatrics, September 28, Town and Country Club, St. Paul, 6:00 P.M.

Upper Mississippi Medical Society Fall Meeting, Pine Cove Inn, Wadena, 3:00 P.M., September 30.

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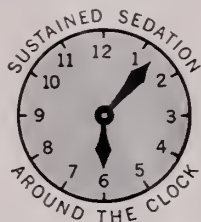
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OFFICE SPACE now available in busy Bloomington. 713 square feet of new space in building with busy group of G.P.'s, dentist and suburban OB-GYN office. Ideal for ophthalmology, ENT or pediatrics. 8040 Penn Avenue South. 888-9211.

WANTED: GP to join clinic serving population area of 12,000. City has new hospital, new clinic building, two nursing homes, new Jr-Sr high school, new swimming pool, rich farming area in Red River Valley. Fishing and hunting nearby; metropolitan city close by. Salary open and partnership if interested. Write or call Warren Clinic, Warren, Minnesota 742-6231, area code 218.

RESIDENCY IN INTERNAL MEDICINE: Applications now being accepted for Medical Residencies at the first, second and third year levels, to begin during the second half of 1967. Active program includes experience in sub-specialties, and participation in a 50,000 visit out-patient clinic, as well as supervised treatment of in-patients. Teaching staff members are all board certified, and the majority hold faculty appointments at the University of Minnesota Medical School. Hospital also conducts residencies in General Surgery, Obstetrics—Gynecology, Radiology, Pathology, Ophthalmology and Urology, and is approved for twelve rotating internships with applications accepted only through the National Intern Matching Program. For descriptive brochure and application blanks, address inquiry to: Chairman of Education and Research, The Charles T. Miller Hospital, 125 West College Avenue, St. Paul, Minn. 55102.

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FOR SALE: Keleket X-ray unit 100 MA. — full wave rectification — table has bucky — four sizes high speed cassettes — contact: Earl Helwig, M.D., 2234 Dunedin Avenue, Duluth 55803.

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GENERAL PRACTITIONER: To engage exclusively in outpatient work on a part-time basis. Regular hours will be arranged to suit convenience of applicant. No night call or weekend work. Contact: D. W. Ferguson, M.D., Veterans Administration Outpatient Clinic, Fort Snelling, St. Paul, Minnesota 55111. Phone: 721-2955, Ext. 256.

WANTED: General practitioner, to join two G.P.'s well established in north central Minnesota community, 2200 pop., 65 miles from Twin Cities. Excellent office space with lab and X-ray, just opened new hospital, all facilities. Assistantship or partnership. Considerable surgery and obstetrics. Hunting, fishing, golf club. Great opening for interested G.P. **WRITE MINNESOTA MEDICINE**—381, 496 Lowry Medical Arts Building, St. Paul, 55102.

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FOR SALE: Mattern X-Ray unit K.V.-60. Good for chest and extremity work. Also an examining table, instrument cabinet, E.K.G., and other equipment. Contact L. A. Whitesell, Jr., M.D., 207 South 1st Street, Buffalo, Minnesota 55313.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X-ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: **MINNESOTA MEDICINE**—289; 496 Lowry Medical Arts Building; St. Paul, 55102.

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INTERNIST, PEDIATRICIAN AND OB-GYNECOLOGIST wanted to join two general surgeons in a rapidly growing practice. Attractive town of 3,000 on large lake 30 miles west of Twin Cities. New 55-bed JCAH hospital with plans for major expansion. Five other physicians in town. No Ob-Gyn., internist, or pediatrician in area. Medical community serves in an area with population of 20-25,000. Planning to expand into partnership multi-specialty clinic. Call or write: Savaryn Clinic, Waconia, Minn. 55387. Telephone: 442-2137.

INTERNIST ASSOCIATE wanted in Pacific Northwest city of 170,000. Low humidity, no ragweed, fabulous recreational area. Expanding practice to accommodate second internist. New multi-specialty building adjacent new hospital in residential area. All hospitals open staff. Further details by correspondence only. Give curriculum vitae first letter. Write: MINNESOTA MEDICINE—382, 496 Lowry Medical Arts Building, St. Paul 55102.

GENERAL PRACTITIONER desires position with group or partnership in town of 3,000 population or more, preferably within 100 miles radius of Twin Cities. Currently in solo practice including surgery and OB at same location for 12 years. Write: MINNESOTA MEDICINE—383, 496 Lowry Medical Arts Building, St. Paul 55102.

IDEAL LOCATION IN SOUTHDAL MEDICAL BUILDING for either primary office or suburban location. Partially furnished and available immediately. Contact: O. A. Schultz, Park Plaza State Bank, phone 935-2141, St. Louis Park.

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FOR RENT: Modern suburban office space now available, with large private parking area, on South Robert near Signal Hills. Successfully occupied by doctors for last twenty-five years. Newly remodeled. Reasonable Rent. 950 South Robert. Telephone: 224-7913, St. Paul.

FOR SALE: 1000 Ft. LAKESHORE located on Big Marine Lake, 28 miles from downtown St. Paul, two level home, 20 ft. living room with marble fireplace facing the lake and the many pine and birch trees. Kitchen with birch cabinets and pecan paneling. Lake-view and dining space, all glass family room, two bedrooms and bath, lower floor has paneled recreation room, with fireplace, second kitchen, bath and shower, laundry room. SECOND HOME—1½ story, full bath, family room, bedroom and fireplace. THIRD HOME is a summer cottage, 24x24 garage, all buildings cedar log siding, bath house on the beach, two wells plus patios. Price: \$49,000.00 Ideal camp site for church, scouts or lodge. For appointment call 297-3320—owner: Russell Stendal.

WANTED: General Practitioner, general surgeon, obstetrician for active group clinic in Minneapolis suburb. Now six man group including full-time surgeon and obstetrician. New clinic facilities and two new hospitals nearby. Salary open. Partnership offered after short trial period.—Coon Rapids Clinic, 9920 Zilla Street N.W., Coon Rapids, Minnesota 55433.

GENERAL PRACTITIONER WANTED: To associate with Physician-Surgeon in Owatonna, A Southern Minnesota community, 25,000 population. Clinic building three years old; with five large treatment rooms; lab.; x-ray; central supply; two doctors' offices; pharmacy; and business offices. Located next door to 85 bed City Hospital. Good opportunity for partnership. Contact: O. W. Roberts, M.D.; 920 So. Cedar St., Owatonna, Minn. Phone 451-4630.

GENERAL PRACTITIONERS AND INTERNISTS to join eight-man group in fascinating San Francisco. Locum tenens also available. Will meet reasonable salary request. A. J. Franz, M.D., 3620 Army St., San Francisco, Calif. 94110.

A man of sixty has spent twenty years in bed and over three years in eating.

Arnold Bennett

Minnesota Medicine at a Glance

Gastric Duplication—Katz et al.

Page 1175

Gastric duplication is a rare congenital anomaly which can be suspected by x-ray and proven only by surgery. The present case describes a rare type of duplication lined with fundic mucosa, arising from the pancreas and communicating with the pylorus and the gastric antrum. This patient had signs and symptoms of acute pancreatitis and chronic intermittent duodenal obstruction. The surgical problem was solved successfully by internal drainage.

Cardiac and Pulmonary Dyspnea—Dines and Parkin

Page 1181

The recognition and differentiation of cardiac dyspnea in contrast to dyspnea due to primary pulmonary disease is an important clinical problem and directly affects the type of treatment instituted. The authors present representative cases illustrating the two types of dyspnea, and outline means of differentiating one from the other. In general, the correct diagnosis is established on clinical grounds; electrocardiographic, x-ray, and pulmonary function studies are used to substantiate the clinical diagnosis.

Cartilaginous Tumors of the Larynx—Gasior and ReMine

Page 1197

An unusual case of chondrosarcoma of the larynx is described in which the patient noted the slow growth of a lateral neck mass of ten years, before surgical removal was accomplished. The literature on this subject is reviewed.

Typical, Atypical and Imitators of Patent Ductus Arteriosus—Lynch

Page 1207

The symptoms, physical signs, and management of the usual (typical) and the unusual (atypical) forms of patent ductus arteriosus vary according to the abnormal physiology produced. In infants, the patent ductus arteriosus is more difficult to recognize than in adults. Surgical closure, even at an early age, is the treatment of choice if the pathophysiology and the status of the pulmonary vasculature permit. Other vascular lesions may mimic a patent ductus arteriosus. Cardiac catheterization and angiography will aid in the differentiation.

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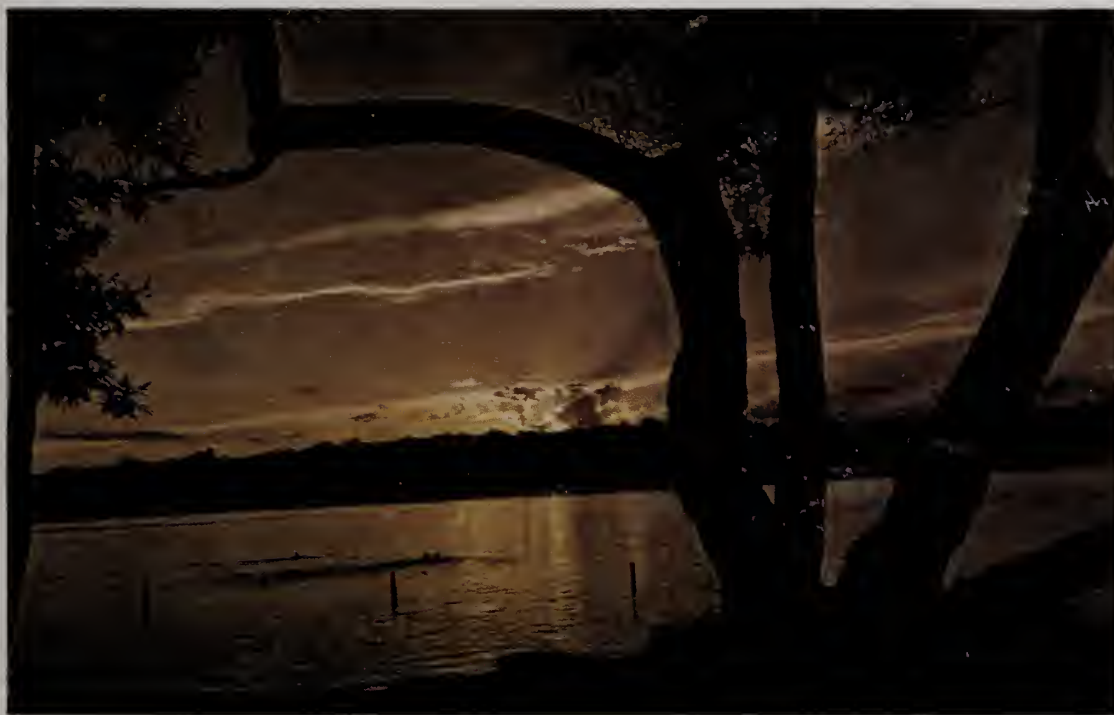
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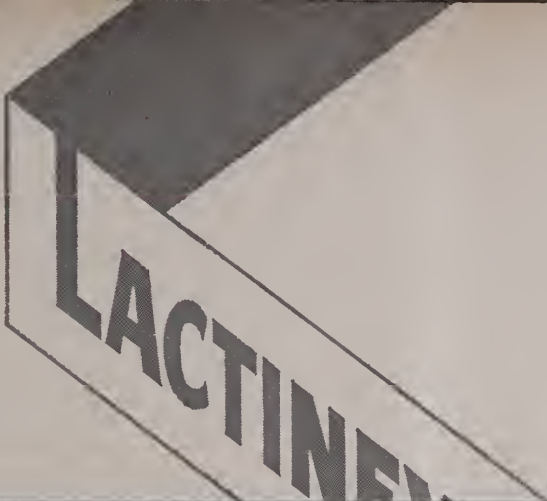
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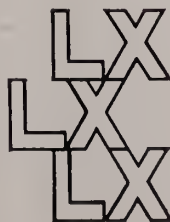
- (1) Siver, R. H.: CMD, 21:109, September 1954. (2) Frykman, H. H.: Minn. Med., 38:19-27, January 1955. (3) McGivney, J.: Tex. State Jour. Med., 51:16-18, January 1955. (4) Quehl, T. M.: Jour. of Florida Acad. Gen. Prac., 15:15-16, October 1965. (5) Weekes, D. J.: N.Y. State Jour. Med., 58:2672-2673, August 1958. (6) Weekes, D. J.: EENT Digest, 25:47-59, December 1963. (7) Abbott, P. L.: Jour. Oral Surg., Anes., & Hosp. Dental Serv., 310-312, July 1961. (8) Rapoport, L. and Levine, W. L.: Oral Surg., Oral Med. & Oral Path., 20:591-593, November 1965.

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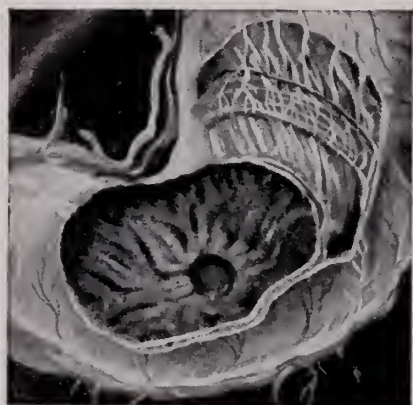
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President's Letter

IN JUNE, 1967, I was privileged to attend an AMPC workshop in Washington, D. C., an even better one than I attended last year. The attending physicians and their wives were supposed to be those most interested in political affairs in their respective states: a hand-picked group, as it were. We were asked to fill out a ballot on preference for President of the United States, as of that particular day, as well as to predict who would be on the Republican and Democratic National Tickets for President and Vice President in 1968. The result of the voting is immaterial. *The real shocker came when our chairman announced that only 47% of those present had bothered to fill out their ballots and turn them in.* And this happened in a meeting of supposedly politically astute and discriminating people. (Yes, I voted!!). I was ashamed of them!!

If we lose our precious political heritage, it will be by default. *We couldn't be bothered!* I want to pass on just a few statistics to you (I don't especially like them either) which really rocked me!

Did You Know That—only 3% of our population work for the candidates for either party? 97% don't want to be bothered!!

Did You Know That—91% had not been contacted to register by either party?

Did You Know That—89% had not been contacted to get to the polls on election day?

Did You Know That—88% had not been asked by either party for contributions?

Did You Know That—76% had not been asked to support candidates of either party?

And Finally, Did You Know That—31% had received no literature from either party?

I know that not everyone can be interested in politics, but certainly, with the educational background each physician (and usually his wife) has, we should be willing to assume positions of leadership in our communities. There are School Boards, Church Boards, Chambers of Commerce Boards, Kiwanis, Rotary, Lions, Women's Clubs (you know the list) that we and our wives can participate in.

Someone has said, "If we are unwilling to participate in the affairs of government, we must then be willing to be governed by less capable persons than ourselves." I want to "point with pride" to one of our County Medical Societies, the Southwestern Minnesota Society. Forty-four physicians out of 54 in that society supported NUHOPE financially. They also promoted the party of their choice. Almost 100% of us physicians are in a favored economic position and can well afford to support not only our own favorite political party and NUHOPE as well; but we can also go further and support generously some of our personal friends who may happen to be candidates.

This doesn't mean that we *Buy These Parties or Candidates!* We can't put them in a straight-jacket just because we have contributed to them; nor is it always even wise to have it known publicly that we support specific candidates financially. **BUT SUPPORT THEM WE SHOULD!!** How much should you give? Only you can tell; but most physicians can easily afford to contribute \$25.00 for themselves, and \$25.00 for their wives to NUHOPE, plus \$100.00 **MINIMUM** to the party of their choice. Most physicians don't have time to engage in political activity; but consider

Continued to Page 1338.

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Enteropathogenic *Escherichia* *Coli* in Children

GERALD M. NEEDHAM, Ph.D.*

JAMES E. WENZL, M.D.**

Rochester, Minnesota

SALMONELLA AND SHIGELLA have long been recognized as agents causing enteric disease, but the role of *Escherichia coli* as an etiologic agent in diarrheal disease, especially in children, has been controversial. Study of the relationship of certain *E. coli* serotypes to infantile gastroenteritis became possible when Kauffman worked out a serologic differentiation. Since there are more than 140 serogroups and many additional serotypes, biochemical tests by themselves were inadequate to differentiate the strains. Subsequently, only a few of the serotypes of *E. coli* were found to be associated with gastroenteritis. These serotypes collectively have been named "enteropathogenic *Escherichia coli*."

Enteropathogenic *Escherichia coli* have been incriminated as causative agents of both sporadic and epidemic gastroenteritis in infants, especially of epidemic diarrhea of the newborn. In infants the mortality of epidemic diarrhea due to enteropathogenic *Escherichia coli* has been reported to be as high as 50%.¹ In other studies, enteropathogenic *Escherichia coli* have been isolated from the stools of full-term and premature newborn infants who were entirely asymptomatic.^{2,3}

Sporadically occurring diarrheal illness due to enteropathogenic *Escherichia coli* appears to be less severe than similar infection seen under epidemic conditions. On the basis of hospital admissions for diarrhea, the reported incidence of sporadically occurring enteropathogenic *Escherichia coli* diarrheal illness in North American infants and children varied from 2.6%⁴ to 45%.⁵ This difference reflects regional variations in both disease prevalence and detection, as well as differences in the age groups surveyed. Table 1 shows the reported incidence of enteropathogenic *Escherichia coli* isolations from the stools of North American infants and children with sporadically occurring diarrhea. The reported incidence is lower for the more northern latitudes and higher for the southern states and Puerto Rico.

*Section of Microbiology, Mayo Clinic and Mayo Foundation.

**Associate Consultant in Pediatric Nephrology, Mayo Clinic and Mayo Foundation.

TABLE 1.

Reported Incidence of Enteropathogenic *Escherichia Coli*
Isolated From the Stools of Children Admitted to
Hospitals Because of Diarrhea

City	Age group	Patients with Enteropatho- genic <i>Escherichia</i> <i>Coli</i> , %
Toronto ⁴	General pediatric	2.6
Denver ⁶	General pediatric	3.1
Kingston, Ontario ⁷	General pediatric	12.7
San Juan, Puerto Rico ³	General pediatric	36.5
Cincinnati ⁸	0 to 14 years	15.3
Cincinnati ⁹	0 to 4 years	30
Atlanta ¹⁰	0 to 2 years	39.4
Columbus, Ohio ¹¹	0 to 2 years	6.3
Oklahoma City ⁵	0 to 19 months	45
St. Louis ¹²	0 to 17 months	40.9
Los Angeles ¹³	0 to 12 months	33.9

This study was designed to test our observation that gastroenteritis due to enteropathogenic* *Escherichia coli* in infants and children seen at the Mayo Clinic was relatively uncommon. We reviewed the results of all stool cultures obtained from infants and children during a 2½-year period, and the medical records of all children with positive cultures for enteropathogenic *Escherichia coli* to define the illness, if any, associated with these organisms.

Materials and Methods

We analyzed 412 consecutive cultures of stool specimens from infants and children, both inpatients and outpatients, chiefly the latter. The period of study extended from June 1, 1964, through December 31, 1966. During this time there were no known epidemics of bacterial enteropathogens. The great majority of stool cultures were obtained because of diarrhea. How-

*See Test Your Word Score Page 1359.

TABLE 2
Clinical Features of 18 Children Harboring Enteropathogenic *Escherichia Coli*

Case	Age, sex	Enteropathogenic <i>Escherichia Coli</i> isolation		Symptoms, signs*	Severity	Treatment	Coexistent conditions
		Type	Month				
1	1 mo, F	0128:B12	Aug.	V, D, F, Dehy.	Severe	Intravenous fluids; chloramphenicol	Congenital hip dislocation; spasticity
2	5 mo, M	026:B26	June	D	Mild	Supportive	
3	4 mo, F	0111:B4	Aug.	D, F	Mild	Supportive	Congenital heart disease
4	2 mo, F	0111:B4	Dec.	V, D, F	Mild	Supportive	Postoperative from gastrostomy for tracheo- esophageal fistula
5	2 wk, F	0111:B4	Aug.	D	Mild	Supportive	
6	12 mo, F	0126:B16	Sept.	D, F	Mild	Neomycin	Congenital rubella syndrome; congenital heart disease
7	14 mo, F	055:B5	Sept.	V, D, Dehy.	Moderate	Intravenous fluids	Iron deficiency anemia
8	3 mo, F	0128:B12	Nov.	D, F	Mild	Supportive	
9	5 mo, F	0126:B16	Dec.	D	Mild	Supportive	
10	10 mo, F	0128:B12	June	V, D, F, Dehy.	Moderate	Intravenous fluids	
11	21 mo, F	0111:B4	Aug.	V, F	Mild	Ampicillin	Acute lymphocytic leukemia
12	11 mo, M	0128:B12	June	D	Mild	Neomycin	
13	3 mo, F	026:B6	May	V, D, Dehy.	Moderate	Intravenous fluids; neomycin	
14	6½ yr, M	086:B7	Sept.	V	Mild	Supportive	Nephrosis
15	11 mo, M	0111:B4	July	V, D	Mild	Supportive	
16	3 yr, M	019:B14	Sept.	None	Asymptomatic	None	
17	2 yr, F	026:B6	July	D	Mild	Neomycin; demethylchlor- tetracycline	
18	3 yr, M	026:B6	Sept.	D	Mild	Neomycin	

*V = vomiting, D = diarrhea, F = fever, and Dehy. = dehydration.

ever, it was not routine practice to obtain stool cultures on all outpatients with diarrhea; in each case the decision was made by the individual physician.

Specimens were obtained for bacteriologic examination from freshly passed stool or by rectal swab. Fecal material was emulsified in a few milliliters of nutrient broth before culturing, whereas material on rectal swabs was inoculated directly onto the various media. All specimens were cultured for enteropathogenic *Escherichia coli* on blood agar plates and on eosin methylene-blue plates. Media specific for isolating *Salmonella* and *Shigella* were also inoculated.

After incubation for 24 hours at 37 C., 10 typical *E. coli* colonies were selected and transferred to a nutrient agar slant. A presumptive screening test was performed based on the reaction of growth from the agar slant with polyvalent OB antisera. Cultures agglutinating with specific *E. coli* OB antisera in the presumptive screening test were confirmed by means of specific *E. coli* O antisera, as follows: growth from the slant was washed off in 0.85% sodium chloride and heated in a boiling water bath for 30 minutes; after the addition of formalin to give a final concentration of 0.5%, the density was adjusted to equal a McFarland Standard No. 3; and serial dilutions of the specific *E. coli* O antisera plus aliquots of the heated bacterial suspension were incubated in a water bath at 50 C. for 18 to 20 hours. Cultures showing agglutinations in dilutions of 1:320 or greater were considered to have the same O antigen as the antisera. This constituted a final serodagnosis.

Organisms considered to be *Salmonella* or *Shigella* were identified by the usual biochemical and serologic procedures.

Results

Enteropathogenic bacteria were isolated from 32 of the 412 cultures, an incidence of 7.7%. *Salmonella* organisms other than *Salmonella typhosa* were isolated in 14 cases (3.4%). No *Shigella* organisms were isolated, and enteropathogenic *Escherichia coli* were isolated in the remaining 18 cases (4.3%). In no instance was more than one enteropathogenic bacterium isolated from the same patient. Table 2 lists pertinent clinical data on the 18 patients from whom the enteropathogenic *Escherichia coli* were isolated.

No predominant serotype of enteropathogenic

Escherichia coli was isolated during the period of study. Types 026:B6, 0111:B4, and 0128:B12 accounted for 13 of the 18 isolations.

All patients were Caucasian and 17 were from the immediate vicinity of Rochester, Minnesota. Also, 12 of the 18 patients were girls. The mean age of boys was 29.5 months and of girls 8.3 months.

Fifteen of the 18 cases occurred from June through September. This may reflect only the increased incidence of viral and nonspecific diarrheas during these months and the consequent increase in the number of stools submitted for culture. During the 2½-year period of study, no enteropathogenic *Escherichia coli* isolations were made from January through April.

Diarrhea was present in 15 of the 18 cases and was the most constant symptom. In no case were the stools said to contain gross blood or excessive mucus. The pattern of diarrhea was not distinguishable from that of nonbacterial diarrhea. Two of the patients who had no diarrhea had vomiting. Seven patients had a temperature of more than 100 F. on initial examination. One asymptomatic boy was discovered to harbor enteropathogenic *Escherichia coli* during a familial contact study occasioned by the isolation of *Salmonella typhimurium* from one of his siblings.

Symptoms were analyzed and estimated to be mild, moderate, or severe: mild, if the patient had vomiting, diarrhea, or both, and showed a favorable response to supportive therapy, consisting primarily of dietary measures; moderate, if the patient received parenteral fluids electively; and severe, if life-threatening dehydration required administration of parenteral fluids. Thirteen patients were judged to have a mild, three a moderate, and one a severe illness. None of those with mild illnesses were treated with antibiotics until after isolation of the enteropathogenic *Escherichia coli* from the stool, usually three to four days after submission of the stool to the laboratory for examination.

Seven patients received antibiotic therapy, six by the oral route. One patient received ampicillin and four neomycin. All were free of symptoms within 72 hours. One patient receiving neomycin continued to have moderate diarrhea after 72 hours. The diarrhea subsided within 24 hours after beginning treatment with demethylchlortetracycline. The seventh patient received intravenous fluids and intravenous chlorampheni-

col; his symptoms regressed within 48 hours. In none of the seven cases could the relief of symptoms be proven to result from antibiotic treatment.

Of the 18 patients, seven (39%) had significant coexisting chronic disease. Six of these seven were girls whose mean age was nine months; this compares with a mean age of 7.5 months for the six girls without coexistent disease. Four of the seven patients had been hospitalized for treatment of the coexisting disease in the month preceding the onset of gastroenteritis symptoms.

Comment

Certain aspects of this study merit further comment. Finding eight of 18 affected children to be less than six months of age is consistent with current concepts of the most susceptible population.^{1,3} Finding 12 of the 18 patients to be female probably has no significance since larger studies have shown a slight preponderance of males.^{7,10} The apparent seasonal incidence may reflect only the greater number of stools cultured during this period of greatest diarrheal occurrence, since other investigators have emphasized the nonseasonal occurrence of enteropathogenic *Escherichia coli*. The occurrence of diarrhea in 15 of 18 cases may reflect case selection as well as symptomatology, since diarrhea is the commonest indication for obtaining a stool culture.

The occurrence of enteropathogenic *Escherichia coli* organisms in infants or children with significant coexistent medical conditions has been emphasized by others.^{1,3} Whether the organisms in those cases were true "opportunists" or were discovered only because of more intensive medical surveillance of known susceptible subjects is open to question. The finding of an increased incidence of enteropathogenic *Escherichia coli* in association with coexistent disease may reflect increased host susceptibility or increased exposure

to hospital organisms during diagnosis and treatment of the coexistent disease.

Without studies to delineate the asymptomatic carrier state in this community, it is difficult to determine the significance of the isolation of these organisms. That 13 of the 18 subjects experienced a mild illness and that eight of the 13 recovered without receiving antibiotic therapy would suggest, that sporadically occurring enteropathogenic *Escherichia coli* organisms were of minor pathogenic significance in this area during the period of this study. Solomon and co-workers¹⁴ in Boston studied 1,078 pediatric patients without diarrhea and found the asymptomatic carrier rate to be 4.7%. They concluded that the frequency of the asymptomatic carrier rate of enteropathogenic *Escherichia coli* makes it impossible to attach causal significance to the isolation of strains of this organism in sporadic episodes of diarrhea. We agree and would emphasize that not all patients with enteropathogenic *Escherichia coli* require specific antibiotic therapy.

Summary

Four hundred twelve consecutive cultures of stool specimens from infants and children with diarrhea were studied for the presence of enteropathogenic *Escherichia coli*. Eighteen positive cultures were found, an incidence of 4.3%. Eight of the 18 patients were less than six months old. The clinical severity of symptoms was mild in 13 cases, moderate in three, and severe in one case. One boy was asymptomatic. Only seven patients received specific antibiotic therapy.

The incidence of sporadic gastroenteritis associated with enteropathogenic *Escherichia coli* was low in this area during the 2½-year period of study. In the absence of a total community study to determine the asymptomatic carrier state, it is not possible to assess the pathogenicity of enteropathogenic *Escherichia coli* in sporadic gastroenteritis associated with it.

References

1. Neter, E.: Enteropathogenic *Escherichia coli* Enteritis. *Pediat Clin N Amer* 7:1015, 1960.
2. Cooper, M. L., Keller, Helen, M., Walters, E. W., Partin, J. C., and Boye, D. E.: Isolation of Enteropathogenic *Escherichia coli* From Mothers and Newborn Infants. *Amer J Dis Child* 97:255, 1959.
3. Riley, H. D., Jr., Start, A. H., Bracken, E. C., Warren, M., Mays, J. E., Jr., and Beargie, R. A.: Enteropathogenic *E. coli* Gastroenteritis. *Clin Pediat (Phila)* 3:93, 1964.
- 4-14. May be secured from the author or the reprints.

Exercise

Whenever I feel like exercise, I lie down until the feeling passes.

—Robert M. Hutchins

Generalized Renal Cystic Disease in Children*

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RENAL DISEASE in children characterized by generalized cystic dilation of the tubules often involves the physician in difficulties of identification, management, prognosis and family counseling. Yet in the confusing body of literature dealing with cystic kidneys there is available information to allow one to isolate and identify many clear-cut pathological and clinical entities and, having done so, to give prognoses and genetic counseling. Recent studies have also suggested reasonable hypotheses to explain the existence and/or development of cystic tubular disease.

Cystic Diseases of the Kidney

Some of the available material is here presented in hope that it may be useful both in practical identification and handling of cystic diseases and in conceptual† thinking of etiology. The table is a list of readily identified cystic diseases. These conditions are discussed below.

Infantile Polycystic Kidney

Infantile polycystic disease is an autosomal recessive condition occurring in infants and progressing to death generally in a matter of hours or days.¹ This disease is characterized by great enlargement of the kidneys, occasionally sufficient to cause dystocia. However, since the cysts are small (1-2mm.), the kidneys are smooth, normally contoured and not lumpy on palpation. The pathological characteristics are sponge-like (Figure 1) cystic dilation of the collecting ducts involving both cortex and medulla, minimal or no increase in connective tissue, and the presence of normal-appearing nephrons (occasionally a small rim of cortex) among the dilated tubules. There is associated bile duct proliferation and cystic changes in the liver and occasionally in the pancreas or lung, but these changes are often of no clinical importance. The clinical findings (large smooth kidney), course (rapidly lethal), pathology (evenly cystic distal nephrons without

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†See Test Your Word Score Page 1359.

dysplasia), and inheritance (autosomal recessive) allow precise identification of this disease.

Microcystic Kidney

Cystic dilation of the proximal tubule may develop during the course of infantile or congenital nephrosis. Unrelenting proteinuria resistant to therapy and progressive renal failure characterize this disease, which is probably primarily due to a glomerular abnormality. When associated with

TABLE I
CYSTIC DISEASES

Infantile Polycystic Kidney
Microcystic Kidney with Nephrosis
Cystic Kidney with Congenital Hepatic Fibrosis
Multicystic Kidney
Medullary Sponge Kidney
Cystic Disease of the Renal Medulla
Cystic Disease with Inherited Syndromes
Polycystic or Cystic Dysplastic Kidneys — Undefined Types

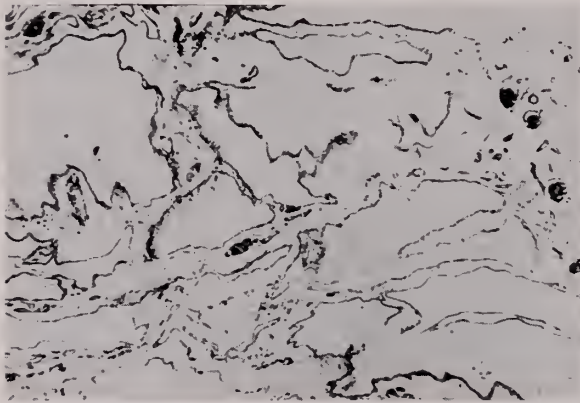


Fig. 1—Infantile polycystic kidney. A few normal glomeruli are set among a network of dilated tubules in loose mesenchymal tissue. H + E $\times$ 100.

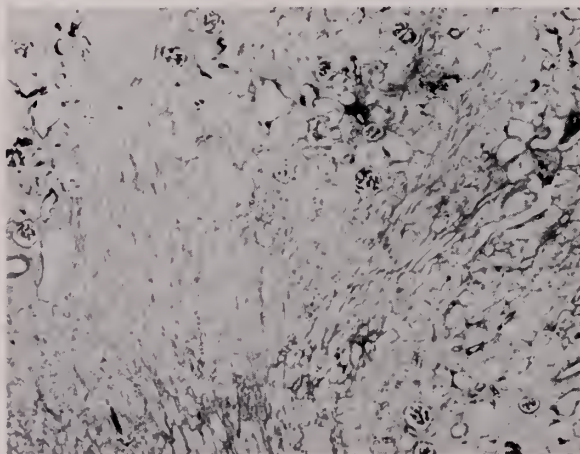


Fig. 2—Autopsy specimen from a 2-year-old child with congenital nephrosis. Dilated tubules are apparent in the cortex but the medulla (lower left) appears normal. H + E $\times$ 100.

prematurity and placental enlargement it is an autosomal recessive condition. Infantile nephrotic syndrome is uniformly fatal unless it can be established that it is secondary to some toxin such as mercury.²

The cystic features must be considered at present as only an interesting pathological finding. They are limited to the cortex (Figure 2), and early in the disease the remainder of the kidney is little changed. The importance of this condition lies not in the cystic tubular changes but in the glomerular abnormality which leads to development of nephrosis.

Cystic Kidney With Congenital Hepatic Fibrosis

Renal tubular ectasia with congenital hepatic fibrosis is an autosomal recessive condition. Large kidneys which show collecting tubule ectasia by pyelography (Figure 3) are associated with liver disease characterized by periportal fibrosis and bile duct proliferation (Figure 4). Patients may present with primarily liver disease—hepatomegaly, cirrhosis, and portal hypertension with varices—or renal disease and arterial hypertension. The distinctive features of the renal disease are enlargement of the kidneys, small cystic tubular dilations in both cortex and medulla, increased connective tissue and progressive glomerular obsolescence (Figure 5). Depending on the stage of the disease, areas with normal glomerular architecture are observed (Figure 6). Many children present with hematemesis due to varices, and the renal disease is discovered incidentally. Prognosis needs to be individualized. While some children die in infancy, others may be asymptomatic and only discovered in families surveyed by pyelography. A period of observation is necessary to determine the rate of progression of the disease, since the children may survive into adulthood.

Multicystic Kidney

When unilateral, a multicystic kidney usually presents as an asymptomatic lumpy mass. The kidney itself is generally enlarged and consists of a nubbin of connective tissue with a few dysplastic nephric elements surmounted by a grape-like mass of large cysts. The findings which allow easy delineation of this entity are the absence of any normal nephron elements, the absence of a renal pelvis, and the almost universal association of ureteral abnormalities, generally atresia

at the hilum. This abnormality is not inherited. There is little evidence that multicystic kidneys need to be removed. Aside from occasional gastrointestinal symptoms due to compression and a case of possible malignant degeneration in a woman in her sixties, they are asymptomatic and benign. The physician's efforts should be bent almost exclusively toward careful examination of the contralateral kidney where correctable obstructive uropathy is reported in as high as 70% of cases.³

Medullary Sponge Kidney

This condition is reported almost exclusively in adults.⁴ However, several case reports in children are available including a description of the classical pathology in an infant.⁵ Furthermore, many radiologists have collected pyelograms in children demonstrating the typical fan-shaped dilated collecting ducts opacified with radiopaque medium occurring in several or all the pyramids. This syndrome is not inherited except when associated with Ehlers-Danlos syndrome*, a dominant condition. Because the disease is limited entirely to the medulla, glomerular function is unimpaired. It is important for the physician to keep this condition in mind since the dilatation of the collecting ducts may progress to small cysts in which concretions may form with subsequent hematuria and/or pyelonephritis. In children, however, this disease must be considered an

*See page 1325.

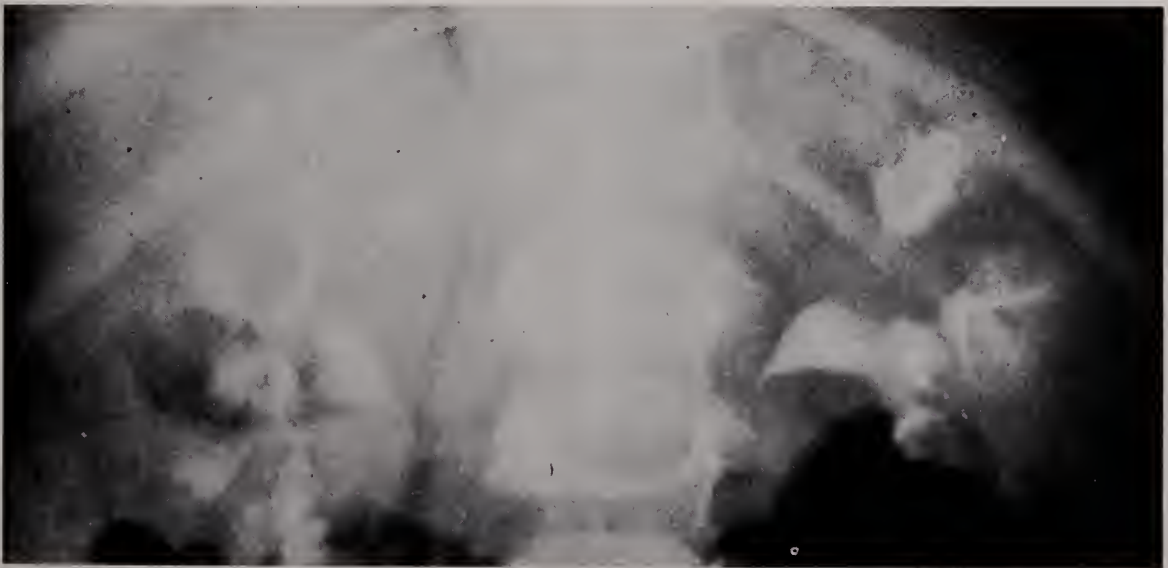


Fig. 3—Intravenous pyelogram of a 9-year-old boy with severe hepatic impairment and varices. The kidneys show generalized enlargement and fan-shaped arrangement of ectatic collecting ducts.

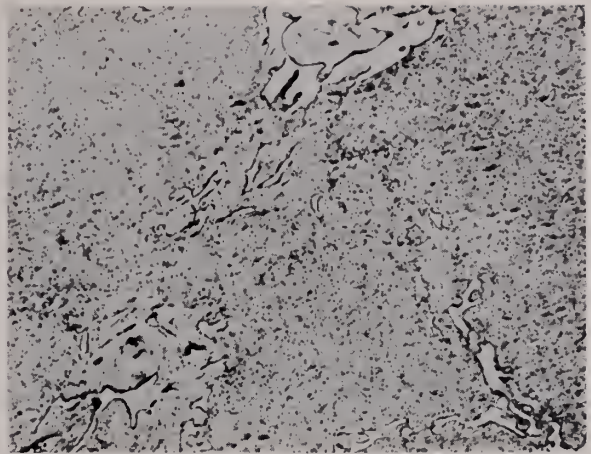


Fig. 4—Liver specimen from a child with hepatic fibrosis and cystic renal disease. There is obvious bile duct proliferation and ectasia with some scarring. H + E $\times 100$.

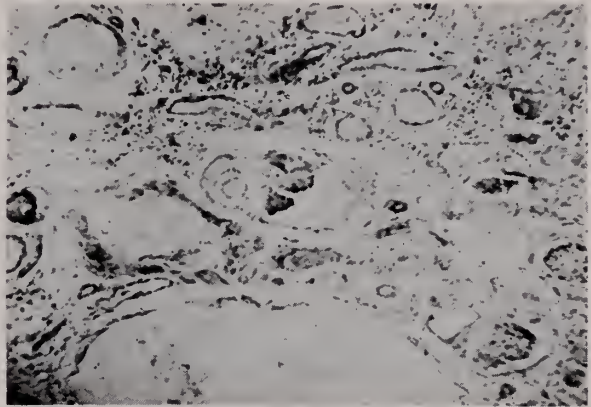


Fig. 5—Section of the kidney from the patient whose liver is shown in Fig. 4. Scarring, glomerular obsolescence, round cell infiltration, and cystic changes are visible. H + E $\times 100$.

interesting but benign structural malformation.

Cystic Disease of the Renal Medulla

Cystic disease of the renal medulla or juvenile familial nephronophthisis, an interesting condition known by both the above names, has been convincingly reported as autosomal recessive⁶ and dominant.⁷ We can suspect this disease in a child who develops polyuria, a nephrogenic defect in concentrating ability, suffers a loss in glomerular function and has a normal urinalysis. Pathologically, the disease is readily recognized. In kidneys which are usually almost normal size, cysts develop in the medulla and, to some extent, in the cortex (Figure 7). The main cortical changes, however, are an increase in connective tissue, round cell infiltration and glomerular obsoles-

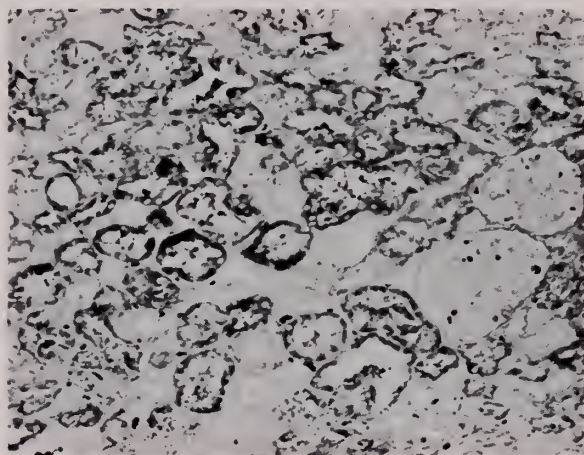


Fig. 6—Percutaneous renal biopsy from the 3-year-old sibling of the patient whose pyelogram is pictured in Fig. 3. The kidney architecture and glomeruli are relatively normal although this patient's pyelogram was similar to that seen in Fig. 3. Azocarmine $\times 100$.

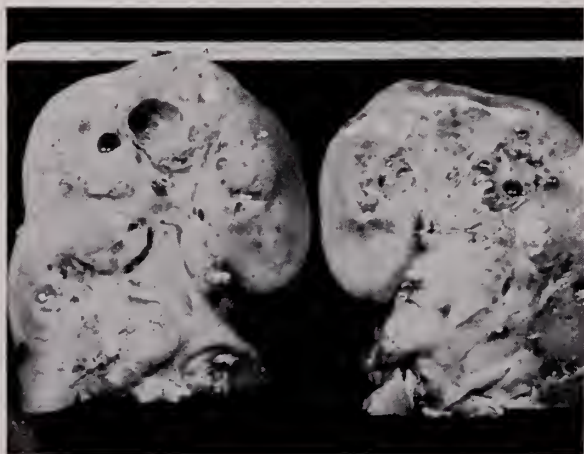


Fig. 7—Nephrectomy specimen from a 7-year-old female with cystic disease of the medulla. The cysts are limited almost entirely to the medulla.

cence. No pyelographic changes have ever been observed. Once established clinically, this condition progresses to renal failure in only a few years. It has been described from early childhood to old age.

Cystic Disease Associated with Inherited Syndromes

Renal disease with cystic components can be classified also when associated with other well-defined syndromes. Examples of this are functioning distal nephron cysts observed in the thoracic asphyxiant syndrome,⁸ a recessive condition which generally has terminated fatally in early childhood due to respiratory disease or uremia, and the association of radiologic evidence of medullary sponge kidney with Ehlers Danlos syndrome.

Diverse Polycystic and Cystic Dysplastic Kidneys

Cysts in any single or multiple areas of the nephron from Bowman's capsule to the collecting duct have been identified in unilateral or bilateral forms of cystic disease in children.⁹ Grossly the pathology ranges from large kidneys identical in appearance to adult late-onset dominant polycystic disease to small dysplastic organs with scattered cystic areas. Often anomalies of other organs are present. Microscopically cystic areas, increased connective tissue, dysplastic or obsolescent nephrons, thickened vasculature, cartilage and smooth muscle, nests of adrenal tissue and the like are found in varying degree. Such kidneys have been identified at ages from the first day of life to older childhood. Occasionally several children with polycystic kidneys in this group are found in one family, implying an autosomal recessive inheritance. The course of disease in such patients varies from rapid fatality (often a result of the associated anomalies) to prolonged periods of well being.

We have observed a child with larger bilateral polycystic kidneys diagnosed in infancy who remains well without azotemia or hypertension twelve years later, although it is generally true that the younger the patient the worse the prognosis. At present, these cystic organs are difficult to separate into meaningful groups; such cases are usually grouped together under the heading polycystic kidneys, undefined type, the prognosis becoming apparent after observation for a time or remaining uncertain.

Laboratory Data

There is relatively little laboratory information which can be brought to bear on differentiating cystic diseases. Routine urinalysis usually is remarkable mainly for its relative normalcy.

Proteinuria and Hematuria

Severe proteinuria occurs in microcystic disease associated with infantile nephrosis, but in most other cystic diseases there is usually no or minimal proteinuria. Formed elements vary in type and quantity with the stage of disease and from case to case but generally are not prominent. It is not meant to imply that severe proteinuria and hematuria do not occur in cystic diseases, but they are the exception rather than the rule.

Concentrating Ability

Glycosuria is seen in scattered instances of some forms of cystic disease such as undefined polycystic kidney or microcystic disease. Limita-

tion of concentrating ability is an early hallmark of cystic disease of the renal medulla, and minor defects in concentrating ability occur early in other conditions such as cystic disease associated with congenital hepatic fibrosis and medullary sponge kidney. Defects in ability to acidify the urine have also been reported in cystic disease of the renal medulla and medullary sponge kidney, but these are not of metabolic significance. Other tubular abnormalities such as salt wasting and amino aciduria are reported in scattered instances but are not considered pathognomonic of any form of cystic disease. Loss of glomerular filtration rate with uremia and associated abnormalities of acid-base and calcium and phosphorus homeostasis occur eventually in all forms of cystic disease described above with the exception of medullary sponge kidney.

Biopsy

Renal biopsy may occasionally be of assistance

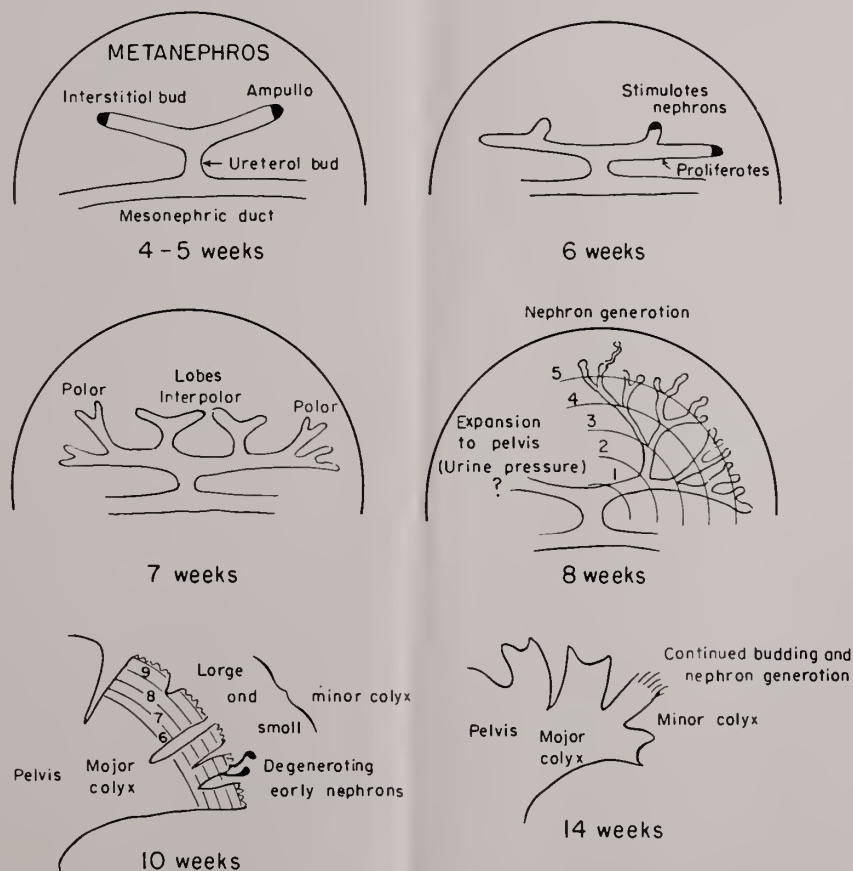


Fig. 8—A schematic presentation, taken from data of Osathanondh and Potter, of human embryonic renal development. Consecutive branching of the ureteral bud, expansion of generations of branches to form the pelvis perhaps due to pressure of urine formed by nephrons newly induced by ampullae, further nephron generation, and some degeneration of early nephrons attached to branches which expand to form calyces, and finally continued budding and nephron induction schematically shown.

in diagnosis. It has helped us in cystic disease of the medulla and microcystic disease, and it is sometimes useful in assessing the stage of the disease and in investigational work. In general, to obtain adequate tissue, open, rather than percutaneous biopsy is carried out if the kidney is involved with large cysts. In our opinion such kidneys with increased connective tissue and thick, poorly contractile vessels which may be close to each other around cysts deserve open biopsy for adequate hemostasis.

Hypertension

As a rule, hypertension occurs only late in the course of cystic disease of the renal medulla or microcystic disease and does not occur in medullary sponge kidney unless pyelonephritis has supervened or in multicystic kidney unless the contralateral organ is abnormal. Other forms of cystic disease may be associated with early onset of increased blood pressure.

Comments

At present, therefore, the clinician can classify his material on the basis of family history (if any), age of onset, intravenous pyelographic picture (or retrograde pyelogram for multicystic kidney) of kidney size and contour, associated abnormalities, some clinical and laboratory data, and occasionally renal biopsy.

It is helpful in considering cystic diseases to be familiar with some of the more recent thoughts on etiology. As a background, Figure 8 composed from data of Osathanondh and Potter¹⁰ summarizes facets of embryonic renal development. In brief, an extension of the mesonephric duct invades metanephric tissue where it branches and proliferates; its distal ends (ampullae) organize nephrons and its interstitial tubular segments grow and expand to form parts of the collecting system. One can visualize¹¹ that, if ampullae are normal, normal nephrons will be developed; but if interstitial segments proliferate excessively, collecting duct ectasia will ensue. The result will

be infantile polycystic kidneys. If ampullae are abnormal, branching and nephron induction are curtailed and interstitial bud growth will lead to cystic structures without attached nephrons. The result will be multicystic kidneys. If both ampullae and interstitial buds are abnormal in varying degree, a variety of forms of cystic renal disease ensue with varying degrees of collecting system ectasia and nephron abnormalities. It is also hypothesized¹¹ that if urinary tract obstruction is present, zones of abnormal nephrons and Bowman's capsular cysts may result. Obstructed cystic kidneys are less homogeneous and therefore are not included in the previous groups of separate entities.

Conclusions

The foregoing does not take into account the development of diffuse cystic tubular disease in previously normal organs such as occurs in certain conditions, e.g., cystic disease of the renal medulla.⁶ In these conditions, it seems reasonable to assume that the kidney responds to tubular cell abnormalities with cyst formation. Undoubtedly many different cellular metabolic defects could generate the same end result just as many glomerular diseases give identical morphologic pictures. This hypothesis could account for the presence of concomitant biliary duct ectasia and renal tubular ectasia by assuming an abnormality in an enzyme system common to both cell lines. The hypothesis is strengthened by the finding of cellular functional abnormalities preceding the development of gross morphologic changes, in experimental cystic diseases, and by the recent discovery that electrolyte abnormalities produce cystic disease in the zone of developing nephrons in normal rabbit neonates.¹² It seems likely that diffuse cystic tubular disease represents a morphological end result of multiple factors. These unknown factors may well involve such things as injury of developing embryonic structures by infectious agents, toxins, obstruction, radiation and metabolic errors, as well as the action of some or all of these on already formed structures in later life.

References may be secured from the author or the reprints.

Experts

An expert is a person who avoids the small errors as he sweeps on to the grand fallacy.
—Benjamin Stolberg

Bronchial Asthma

Food,
Inhalant,
Drug
and
Chemical
Allergies
in
Its
Etiology

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WE ARE CONTINUING to obtain evidence which lends support to the thesis that food, inhalant, drug and chemical allergies are responsible for practically all bronchial asthma and other respiratory clinical allergies.^{1,2,3,4} Data based upon clinical results recorded in our practice indicate that food allergy is the sole cause of respiratory manifestations of allergy in 20 to 40% of all cases. Allergy to pollens as the sole cause is indicated in 3 to 25% according to age and degree of inhalation, the minimum frequency appearing in infancy. Associated food and inhalant allergies, one or the other being dominant, are responsible in 42 to 53%.¹ When these allergies are recognized and controlled, infectant asthma, intrinsic and psychogenic causes assume a minimal role or become non-existent. Hence, we have found that change in location or climate, prolonged sanatorium care or long-term corticosteroid therapy is not required to control bronchial asthma.

History of Asthma Due to Food Allergy

Recurrent Attacks With Nasal Symptoms

It is important to recognize the typical history of bronchial asthma due to food allergy,^{1,2,4} especially in infants and children. The typical history consists of recurrent attacks of asthma often preceded by or associated with nasal symptoms. Vomiting and fever as high as 104°F. may occur. Severe or moderate asthma continues for one to three days. Wheezing and coughing disappear in the subsequent one to five days. We have observed a definite decrease or absence of symptoms in the summer.⁵ When food allergy is not recognized and controlled for several months, the interim relief between recurrent attacks is replaced by moderate coughing and wheezing.

Because of initial nasal symptoms and fever in approximately 50% of these cases, infectant asthma incorrectly becomes suspect by many physicians. Relief of this asthma with our control of food allergy has reduced such possible infectant asthma^{1,2,9} to a minimum or eliminated it entirely. When this typical history is present, control of food allergy relieves the symptoms with

no vaccine therapy, no desensitization to skin-reacting inhalants and no long-term corticosteroid therapy.

Interim Relief Between Attacks

Interim relief between recurrent attacks^{1,2} in the typical history is similar to the refractoriness to injections of an allergen after it has produced anaphylactic shock in the guinea pig. During the patient's attack antibodies to causative foods in the lungs can be assumed to be inactivated by uniting with the blood-borne allergens of the foods. Thus their continued ingestion causes no asthma until the antibodies reaccumulate above an assumed reacting threshold in the lungs. Our study of asthma due to food allergy indicates that food allergy is the usual cause of recurrent cyclic attacks in all ages. Such refractoriness after asthma due to inhalants is rare, as evidenced by continued daily asthma as long as causative pollens or other inhalants are in the air.

Although this typical history occurs in some adults,¹ an equivalent history due to food allergy is more common.

Such asthma is perennial and continues in varying degrees, particularly from 1:00 to 5:00 a.m. and with exercise. Careful interrogation often reveals exaggeration of symptoms every two to four weeks, especially in the fall, winter and early spring when food allergy, we have found, is usually exaggerated.

Emphysema and Chronic Bronchitis

The results we obtain in our practice increasingly substantiate the frequency of inhalant and especially food allergy in the causation of the obstructive symptoms of emphysema and chronic bronchitis. Our patients have been relieved of the invaliding symptoms of emphysema as their allergies, particularly to foods, have been brought under control. We have used minimal or no bronchodilator, corticosteroid and intermittent positive pressure-breathing therapy. Our results indicate that bronchospasm and bronchorrhea are due to uncontrolled allergy rather than to actual destructive changes in the lungs. Twenty patients in whom symptoms of emphysema have been brought under good or excellent control with the study and treatment of allergy especially to foods have shown slight or no improvement in their pulmonary function tests.⁶

This important role of food allergy has been confirmed in a recent contribution in which 60 cases of obstructive emphysema with similar relief are reported. In 42 of these cases the degree of destruction in the lung has been indicated by lung scanning¹⁰ with the use of I¹³¹ in human albumen by vein.

In the recent European symposium⁷ on bronchitis and emphysema the asthmatic predisposition was recognized. A further indication of allergy in the etiology of these diseases is the presence of eosinophiles in the sputum and bronchial tissues of affected individuals.⁷ Herxheimer⁸ states that "most emphysema is bronchial asthma with a different symptomatology." Banyai⁹ concludes that bronchial asthma is a major factor in the obstructive symptoms of emphysema.

Indications of Food Allergy

History

Food allergy is usually suggested in the patient's history. The typical history of asthma^{1,2} due to such allergy must be recognized. Perennial asthma, especially in older patients, evidenced by recurrent exaggeration in the fall, winter and early spring and by decrease of symptoms in the summer, requires study of food allergy. Foods which exaggerate asthma or other clinical manifestations of food allergy may be known to patients.

Dislikes and disagreements for specific foods are due to allergy in 20 to 30%.¹¹

Since diet diaries are rarely accurate,¹ their recording by patients and their analysis by physicians are of questionable help.

Skin Testing

Though scratch tests often fail to reveal any or all foods causing clinical allergy, they are routine in our practice.¹ This procedure is justified by large reactions which often occur to foods causing immediate symptoms. Smaller reactions less frequently indicate clinical allergy, often being non-specific. It is generally agreed that much chronic cumulative food allergy is not indicated by positive skin tests.

The clinical importance of all skin reactions, including the large ones, must be determined by provocation feeding tests, necessarily in the symptom-free patient. Such tests, however, may not correctly incriminate an allergenic food if per-

formed during refractory periods between attacks due to food allergy or during the summer when food allergy is often inactivated.⁵

Failure to realize the fallibility of skin testing with foods in revealing clinical allergy and the continued use of test-negative diets to study such allergy rather than diet-trial explain in large part the unfortunate failure of many allergists and other physicians to recognize the frequent clinical manifestations of food allergy.

It is important to eliminate all cereals in the initial study of food allergy in bronchial allergy. Bakery products are made of soy and potato starch flour according to published recipes.^{1,7} Though allergy to soy does occur, its occurrence is much less frequent than allergy to cereal grains. Diarrhea in infancy from allergy to soy is well known. This led to our inducement of meat packers in 1940 to make strained meat¹⁴ which can be used in a meat-base formula^{14,15} without animal and soy milks and which can be prepared in the home or purchased from Gerber Company.

Occasional allergy to soy in adults was evidenced in one man, in whom chronic asthma and symptoms of obstructive emphysema were not relieved until soy, as well as cereals, milk, egg and other foods were eliminated from his diet.^{1,15} When soy bakery products are distasteful, especially to children, they are omitted. Then potato, tapioca, sugar, along with milk-free butter,^{1,7} are increased to maintain nutrition and weight. Provocation tests with other foods are made when relief occurs, as advised above.

Intradermal tests with foods are not used routinely in our work. Many reactions, especially with the intradermal method, are due to irritants in the food extracts. Death, moreover, has been reported from intradermal tests with foods.^{12,13}

Control of Food Allergy

When food allergy is indicated, our cereal-free elimination diet^{1,3,15} is ordered on the first conference in office or hospital. Since test-negative diets rarely reveal or control food allergy, they are not used.

Elimination of Asthma-Producing Foods

Good results from this diet depend on the initial total elimination of all cereal grains including wheat, as well as of the most frequent food

to cause asthma—milk, and also of egg, chocolate, fish, coffee and less allergenic foods. Patients must be given a list of allowed foods including a milk-free hydrogenated* soy oil as a butter substitute.¹⁵ They should be supplied with menus and recipes for soy-potato bakery products. Bakery products must be made at home or bought from reliable bakers who are supervised by the physician.^{1,15} We have found that gluten or even small amounts of wheat, not listed on the label, in bakery products prevent relief in wheat-sensitive patients.¹⁷ Maintenance of nutrition and desired weight is mandatory.

Provocative Tests

The strict initial diet must be maintained until two expected attacks of asthma have not occurred in the fall to late spring or until perennial symptoms have been relieved for one to two months. Then, provocation tests with additional vegetables and fruits, each to be added every two to four days, and later with separate cereals, egg, coffee, milk and other foods are indicated. If symptoms recur without breaks in the diet, foods added in the preceding one to two weeks must be excluded.

It must be remembered that foods tolerated in the summer may cause symptoms in other seasons.⁵ Food allergy often causes recurrent "colds," chronic bronchitis or bronchial asthma during the fall, winter and spring. When allergenic foods have been eliminated for one to three years, lasting tolerance may arise to some or all foods, especially in children. This tolerance occurs infrequently in adults.

Hypodermic desensitization to foods has failed.

Diagnosis and Control of Inhalant Allergy

Inhalant allergy is indicated by asthma during pollen seasons or from animal emanations, dusts, fungi or other air-borne allergens.¹ Though it is a sole cause of asthma less frequently than food allergy, it has been associated with food allergy in approximately 42 to 53% of our cases.

When suspected, initial scratch tests with all important inhalant allergens should be routine. Intradermal tests may be omitted, but if done, they should be performed only with inhalants which have given negative or one plus scratch tests. They should not be done with cottonseed

*See Test Your Word Score Page 1359.

or flaxseed, or with dilutions stronger than 1 to 500.¹ As with foods, all positive inhalant reactions do not indicate clinical allergy. History or provocative inhalant tests must determine their allergenicity. Thus, reactions to trees, grasses and fall pollens may occur in a patient allergic only to the fall pollens. Desensitization too often is given empirically with pollens, fungi, dusts, or other inhalants for months or years with no relief to patients suffering with unrecognized food allergy alone.

Treatment of Inhalant Allergy

Environmental control often relieves allergy to animal emanations, dusts and other allergens in the living or working environments. Efficient pollen and dust filtration reduces or controls resultant symptoms.¹

When the elimination of inhalant allergens is impossible, desensitization to antigens containing the responsible inhalants is indicated.

Drug and Chemical Allergies

Drugs and chemicals as causes of asthma are rare when compared to their role in the production of allergic manifestations in the skin and to a lesser degree in other tissues. Acetylsalicylic acid causes asthma in approximately 3 to 5%¹³ of these cases. It is necessary, of course, to eliminate totally the use of a drug or chemical when its allergenicity has been demonstrated. Though other pain-relieving drugs cause clinical allergy, they infrequently cause asthma. Asthma and fatal anaphylaxis occur from penicillin of all types and occasionally from other drugs.¹ One of our patients developed severe near-fatal asthma three times before tolbutamide was recognized as the cause.

Evidence Against Infectant Asthma

When food allergy is controlled, recurrent nasal symptoms,^{1,2,16} at times accompanied by fever of 101 to 104°F. suggesting an infectious cold, associated with or followed by bronchial asthma, do not occur. Their recurrence in September to November, especially in children, is best explained by activation of food allergy in the fall months.⁵ Tonsillectomy and adenoidectomy, rather than alleviating asthma, may serve to intensify it. When asthma due to food allergy

is controlled, infectious colds do not cause asthma.

We have found that vaccine therapy alone does not control asthma.

Drug Therapy

Until the control of food and/or inhalant allergy relieves asthma, medications are required.^{1,3,4} Epinephrine, 1 to 1000, hypodermically in doses of 0.15 cc. to 0.5 cc. according to age, every one-half to six hours, is most effective. Inhalation of epinephrine 1 to 100, or isuprel 1 to 200, by hand atomizers or by intermittent positive pressure is also justified. Aminophyllin, 2 to 7½ grains, by rectum or by vein after the age of five years, in doses according to age, can be given every eight to 12 hours. Ephedrine and aminophyllin in tablets or suspension relieve moderate asthma.

For severe and intractable asthma large doses of corticosteroids orally or intramuscularly are indicated. The doses are reduced to a minimum or entirely eliminated as the immediate and continued study of inhalant and food allergy controls the symptoms. If corticosteroids have been given previously on a long-term basis, small doses may be required as compensation for impaired adrenal function. When causative allergy has been controlled, long-term corticosteroid therapy has not been required in any child and in only small doses in a small percentage of adults in our practice. Indicated potassium therapy and, if duodenal ulcer is possible, antacid therapy may be advisable. In severe or intractable asthma electrolyte and fluid requirements must be fulfilled.

Mild or moderate asthma from uncontrolled inhalant or food allergy is relieved by small oral doses of ephedrine and aminophyllin. Epinephrine hypodermically or by inhalation or isuprel by mouth or inhalation is also helpful. A brief course of corticosteroid therapy may be advisable. In our practice no long-term intermittent positive pressure has been used. The relief of asthma and of associated emphysema and bronchitis has depended upon control of allergy to inhalants, drugs, chemicals, and especially to foods.

Summary

1. A typical history of bronchial asthma due to food allergy in children and in some young adults, and its equivalent perennial history in adults, must be recognized.

2. Food allergy is observed to be the sole cause of bronchial asthma in approximately 20 to 40% of cases and is associated with inhalant allergy, as a major or minor cause, in an additional 42 to 53%. Inhalant allergy is the sole cause in 3 to 25% according to age.

3. The invaliding symptoms of emphysema and chronic bronchitis decrease even to a minimum with little or no bronchodilator or corticosteroid therapy when atopic allergy to foods, at times associated with inhalant allergy, is controlled. This relief results from control of bronchorrhea and bronchospasm due to atopic allergy. Since little or no improvement in pulmonary function

tests occurs, relief is not due to a decrease in destructive lung disease.

4. Food allergy is studied and controlled with the writers' cereal-free elimination diet.

5. Control of inhalant allergy requires desensitization to allergens unless the causative inhalants can be eliminated from the patient's environment.

6. Until control of food and/or inhalant allergy occurs, symptoms must be relieved by medications, as advised. These medications are also given for asthma arising from subsequent breaks in diet, allergy from drugs, or inadequate control of inhalant allergies.

References

1. Rowe, A. H. and Rowe, A. Jr.: Bronchial Asthma—Its Diagnosis and Treatment. Charles Thomas, Springfield, Illinois, 1963.
2. Rowe, A. H., Rowe, A. Jr. and Young, E. J.: Bronchial Asthma Due to Food Allergy Alone in Ninety-Five Patients. JAMA 169:1158, 1959.
3. Rowe, A. H. and Rowe, A. Jr.: Bronchial Asthma—Its Treatment and Control. JAMA 172:1734, 1960.
4. Rowe, A. H. and Rowe, A. Jr.: Bronchial Asthma in Infants and Children Due to Food and Inhalant Allergies. Asthma Research 4:189, 1967.
5. Rowe, A. H. and Rowe, A. Jr.: Seasonal and Geographic Influences on Food Allergy. Int Arch Allerg 13:233, 1958.
6. Rowe, A. H.: Seasonal and Geographic Influences on Food Allergy. J Allerg 13:55, 1941.
7. Rowe, A. H. and Rowe, A. Jr.: Food Allergy—Its Role in Emphysema and Chronic Bronchitis. Dis Chest 48:6, 1965.
8. Orie, N. G. and Shister, H. J.: Bronchitis. An International Symposium, C. C. Thomas, 1961.
9. Herxheimer, H.: Eosinophiles in Sputum of Patients with Asthma and Emphysema. Excerpta, Medica, International Congress Series, No. 42, 1961.
10. Banyai, A. L.: Bronchial Asthma as Cause of Obstructive Emphysema. Ann Allerg 23:10, 1965.
11. Lopez-Majano, V., Tow, D. E. and Wagner, H. N. Jr.: Regional Distribution of Pulmonary Arterial Blood Flow in Emphysema. JAMA 197:2:121, 1966.
12. Vaughan, W. C. and Pipes, D. M.: Is There a Correlation Between Food Dislikes and Food Allergy? J Allerg 8:257, 1937.
13. Swineford, O.: Anaphylactic Shock from Skin Testing, Two Cases—One Fatal. J Allerg 17:24, 1946.
14. Vaughan, W. C.: Practice of Allergy. 3rd Edition, C. V. Mosby, 1954.
15. Rowe, A. Jr. and Rowe, A. H.: Strained Meat Formulas in Allergic Diseases of Infants and Children. Calif Med 81:4:279, 1954.
- 16-18. May be secured from the author or the reprints.

Ehler-Danlos Syndrome

This disorder is usually familial, congenital and is inherited as an incomplete dominant. It may affect either sex.

It is characterized by hyper-elasticity of the skin, hyper-laxity of the joint, subcutaneous tumor, and fragility of the skin and its blood vessels with faulty healing leading to papyraceous* scar formation. It is frequently associated with other organic disorders. The features of this disease are evident in childhood and persist throughout life. Because of the exceptionally thin and fragile skin, precautions directed towards the prevention of injury should be undertaken.

Durham, Robert H.—Encyclopedia of Medical Syndromes
Hoeber Medical Division, Harper and Row, New York

*See Test Your Word Score Page 1359.

Heart

Nature is profoundly imperturbable. We may adjust the beating of our hearts to her pendulum if we will and can, but we may be very sure that she will not change the pendulum's rate of going because our hearts are palpitating.

—Oliver Wendell Holmes

Memoirs of a Lady Ambulance Surgeon

Jim, Stockings, Babe, and Don

The old ambulance stable is one of the most fascinating memories of my hospital days, and nothing quite like it exists today. Since the earliest dawn of civilization man has turned to two faithful companions, his horse and his dog, for help in time of stress, either to save his own life or to help him on some errand of mercy.

When you entered the building you could see the stalls with the sleek contented animals, and hear that indefinable crunch of eating good oats, and smell the also indefinable fragrance of hay, plus horse, which one associates with a well kept stable. If you wandered near the stalls, the keen eyes of these trained horses seemed to be taking you in completely with an accurate appraisal.

Remarkable animals they must have been, for today they stand out in memory as sharply as though I had seen them yesterday. There was Jim, white and graceful, distinctly of the racing horse type, and the fastest of them all. High-spirited, sensitive, loyal, Jim would do anything that his master called upon him to do, but he wanted to do his part freely and generously and without coercion. All that was necessary was to take the reins and give a click, and Jim would be off top speed wherever he was directed.

Stockings in the next stall, gave Jim a close brush for first place in our affections, and I do believe that in the heart of at least one of the drivers he held that place. Stockings, though heavier in build, also had tremendous speed; a bay with white feet, he had the uncanny intelligence that could cut corners, and jump children at play, and get you to your destination sound of wind and limb.

Next to him was big and rollicking Babe, well-named in that he lacked mature judgment. I was in only one accident during my entire experience on the ambulance and that was when our casual Babe was taking us down a crowded side street. He encountered a still more casual horse attached to a grocery wagon. They met in a head on collision and we all swung around in a mighty whirl, each driver finding himself heading in the opposite direction. After sorting ourselves out and finding that no one was hurt, we proceeded on our way.

Don occupied the last stall. He was a big, gaunt, surly, iron-gray horse. If he had been a human, you would have been sure that he suffered from chronic indigestion. He was cynical, not vicious, but bored to death to be called upon too often for speed. However, when it was necessary, old Don could get up speed, and when he really went into action he was tremendous with his huge ungainly body plunging along in the crowded streets.

How can I recreate for those who have no memory of it the fascination of those days when New York was a horse-drawn city?

Emily Barringer, M.D.: Bowery to Bellevue, 1950.

It is not open to the cool bystander . . . to set himself up as an impartial judge of events which would never have occurred had he stretched a helping hand in time.

—Winston Churchill

Adversity introduces a man to himself.—Anonymous

Nonspecific Ulcers of the Colon

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THE SIMPLE OR nonspecific ulcer of the colon is a relatively rare lesion which occurs much more commonly in the cecum and ascending colon than elsewhere. It may mimic other more common gastrointestinal diseases clinically and be confused with these diseases. Pathologically, it is a simple inflammatory lesion which may be confined to the mucosa and submucosa but has a tendency to penetrate more deeply, leading to perforation. Nonspecific inflammatory reaction is found in the base of the ulcer and there is often a considerable local reaction surrounding the crater, with a tendency to scarring and sometimes contracture leading to partial obstruction. It is unrelated to granulomatous disease of the colon, ulcerative colitis, vascular disease, and infectious disease. No aberrant mucosa has been reported in the area of ulceration. For the most part the literature has been devoid of an adequate description of this entity and there is only a single previously reported case in which the diagnosis was suggested preoperatively.¹

Nonspecific ulcer of the colon was first described by Cruveilhier² in 1830. A review of the literature discloses only 90 cases reported since then (Table 1). Most of the authors suggest that the disease is more common than is generally realized and that it is missed completely or misdiagnosed in many instances. It occurs predominantly in males in a ratio of 2 to 1. The age range is wide, varying from 18 to 80. In males the peak incidence is in the fifth decade, while in females it is in the third decade.³ Approximately 4% of the reported patients were known to have peptic ulcer of the stomach or duodenum.⁴

Clinical Findings

Appendicitis-like Symptoms

In the vast majority of cases pain is the presenting symptom. The pain is quite variable and may be acute; or it may be relatively chronic with

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an insidious onset. In uncomplicated cases the clinical findings often simulate those of appendicitis. There is right lower quadrant pain and tenderness, often with an acute onset but sometimes recurrent and usually unrelated to meals. This clinical picture occurs when the ulcer is in the cecum. In Barlow's series of 78 cases⁴ constipation was reported in 40%. In this group the initial diagnosis was appendicitis in more than two thirds of the patients. Rectal bleeding or melena has been reported in a total of five cases.^{3,5} The bleeding is usually not very serious. The typical clinical picture is altered by complications, the most significant of which is acute perforation. This occurs either into the peritoneal cavity resulting in peritonitis or into the retroperitoneal space causing a retroperitoneal abscess. In single instances the patient presented with an intussusception³ and a subphrenic abscess.⁶

Location of the Ulcer

Nearly two thirds of the ulcers were found proximal to the transverse colon, most commonly in the cecum (44 cases), accounting for the frequent incorrect presumptive diagnosis of appendicitis. The sigmoid colon was involved in 16% of the total cases. This relatively high incidence of ulcers near the ileocecal valve is similar to the situation in the duodenum where ulcers occur beyond the pyloric sphincter where the blood supply is relatively poor according to Cameron.⁷

Perforation

Perforation is an exceedingly common complication, particularly in ulcers involving the left colon. Barlow⁴ found that 81% of the lesions in the left colon had perforated at the time of surgery or autopsy; perforation was slightly less common (66%) in lesions of the proximal colon.

Pathologic Findings

Grossly the ulcer of the colon resembles a peptic ulcer with smooth, punched-out margins or an irregular, sharply raised border, varying in size up to 4 cm. in diameter. The shape also varies and, if elliptical, the long axis may be either longitudinal or circumferential. The crater may extend to the serosa with destruction of the muscle layers and marked overgrowth of the connective tissue resulting in thickening of the contiguous bowel wall. The base is often necrotic and in-

filtrated with inflammatory cells, and there is frequently considerable inflammatory response in the bowel surrounding the ulcer. Multiple ulcers were found in 18 of the 90 cases reported and were invariably situated in close proximity to each other.^{3,4,6,8} The inflammatory reaction was often severe enough to produce pseudotumor; therefore the lesion has been misdiagnosed, surgically, as a carcinoma in a number of instances (e.g., our Case 2).

Roentgenographic Findings

There is very little information in radiologic literature regarding this entity, and in only a single previous case report was the diagnosis sug-

TABLE I
SITES OF NONSPECIFIC ULCERS OF COLON

Cecum	44
Ascending	17
Hepatic flexure	6
Transverse	2
Splenic flexure	3
Descending	4
Sigmoid	10
Rectum	4
TOTAL	90 Cases



Fig. 1-a — Initial barium enema showing poor filling of the ascending colon due to spasm. The ulcer is not well visualized and the deformity suggests more extensive disease than is present.

gested preoperatively.¹ In most of the cases in which roentgenographic findings were reported, they tended to be misleading. The spasm usually found in conjunction with the lesion, along with its accompanying poor filling and the irregular appearance of the involved bowel, suggested either carcinoma or tuberculosis in the majority of cases^{4,6,9}

Feldman¹⁰ indicates that the lesions are very difficult to find and suggests the use of double contrast enema to outline the ulcer crater. In summarizing the roentgen signs of nonspecific colon ulcer, he listed the following roentgen signs: (1) a visible ulcer defect, (2) nodular swelling due to edema surrounding the ulcer, (3) localized irritability of the affected portion of the colon, (4) localized hypermotility of the bowel, (5) localized spasm and tenderness, (6) stricture and stenosis due to cicatricial changes, (7) perforation with signs of intraperitoneal air.

Case Reports

Case 1

The patient, a white female, 20 years of age, was ad-

mitted to University Hospitals in April 1965 with symptoms of abdominal pain and melena for the preceding two months.

Past History

The patient, her mother, and two sisters had incontinentia pigmenti, a familial disease with cutaneous and dental abnormalities; and the stigmata of this disease were also apparent on examination.

Her rather involved medical history revealed that she had suffered recurrent episodes of abdominal pain since childhood. These were frequently associated with bloody stools and always responded to conservative treatment. An extensive hospital workup elsewhere in November 1954 included a barium enema and an upper G.I. series with a small-bowel study. These procedures did not reveal the source of her difficulty.

In March 1955 she underwent a laparotomy at another hospital for suspected appendicitis. The appendix was removed but was normal and no other findings were reported. She was again hospitalized in March 1956 following an episode of pain and bloody diarrhea which lasted 24 hours. Again the cause was not determined. In December 1961 she was rehospitalized elsewhere with anemia and a palpable right lower quadrant mass. Tumor was suspected and she was explored. A benign 2-cm. ulceration on the lateral aspect of the cecum, just below the level of the ileocecal valve, was found; and a segment of the cecum measuring approximately $2\frac{1}{2} \times 4$ cm. was removed. This was a wedge type of local resection.



Fig. 1-b—This film was taken 90 minutes after oral administration of barium. The ulcer crater is visible (arrow) and the marked scarring and shortening of the right colon is apparent. The previous resection removed only a small $2\frac{1}{2} \times 4$ -cm. wedge of cecum.



Fig. 1-c—Spot film of the hepatic flexure demonstrates the ulcer to good advantage. Note the scarring as well as redundant folds opposite the crater.

On the present admission the patient stated that she had been well for a time after the surgical procedure.

Physical and Laboratory Findings

There was considerable tenderness to palpation in the right lower quadrant associated with muscle spasm and slight rebound tenderness. Pelvic and proctoscopic examinations were negative. Her hemoglobin was 9.9 grams and the stools were guaiac positive.

Stool examinations for ova and parasites, and cultures for Shigella, Salmonella and Staphylococcus were negative.

Radiographic Studies

Initial radiographic studies in an attempt to find the pathology by barium enema were unsuccessful because of marked tenderness and irritability of the right colon which prevented adequate retrograde filling. It was therefore elected to visualize the colon following oral barium administration. This resulted in satisfactory demonstration of a single ulcer at the hepatic flexure associated with considerable fibrosis and scarring (Figure 1).

Surgical Findings

Because of the extremely chronic nature of the patient's illness and the extent of her present symptoms, surgery was considered necessary, and a right hemicolectomy was performed. At surgery the wall of the ascending colon and hepatic flexure showed generalized thickening. There was a striking foreshortening of the inner aspect of the colon with thick redundant folds on the opposite wall. Induration along the medial aspect prevented palpation of the ulcer. The right colon and 8 cm. of the terminal ileum were removed (Figure 2).

Pathologic Observations

Microscopic examination (Dr. Walter Jaeschke) showed a marked inflammatory reaction composed mainly of



Fig. 2—Photograph of the gross specimen. The ulcer is indicated by the arrow. The surrounding mucosa is normal but somewhat congested. The short attached segment of terminal ileum is also normal.

lymphocytes and plasma cells which infiltrated the entire bowel wall. The base of the ulcer was filled with fibrinous debris, granulation tissue, and acute and chronic inflammatory cells. The regional lymph nodes showed reactive hyperplasia and, in some areas, microabscess formation. There was no evidence of malignancy, and special stains for fungi and acid-fast bacilli were negative.

The patient recovered uneventfully.

Review of the surgical specimen obtained in December 1961 disclosed a similar picture. The ulceration extended nearly to the serosa which was exceedingly congested and inflamed. Lymphocytes and plasma cells predominated with some eosinophils also evident; no epithelioid cells were found and parasites were not identified.

Case 2

The patient, a twenty-five-year-old male, was seen with a chief complaint of right lower quadrant pain.

X-ray Findings

Barium enema examination revealed a large ulcer near the base of the cecum with what appeared to be an associated partially encircling mass deforming the cecum. The ulcer extended medially to the margin of the ileocecal valve. The remainder of the colon and the terminal ileum were normal (Figure 3).

Surgical Observations

The patient was operated upon, and at surgery a rubbery mass was found involving the cecum. The right colon was resected. Grossly it was impossible to tell whether or not the mass was a tumor. On opening the specimen there was gross thickening of the bowel wall. The base of the ulcer was identified; it was yellow-gray in color, obviously necrotic, and the surrounding mucosa was inflamed but otherwise normal. The adjacent serosa appeared congested and covered by granular, thin red exudate. Histologic examination showed only nonspecific ulceration with acute and chronic inflammation and occasional giant cells suggesting a foreign-body reaction. There was no malignancy. Examination of the regional nodes showed only lymphadenitis.

When seen six months later the patient was entirely asymptomatic. A repeat barium enema showed no evidence of recurrent disease.

Discussion

The natural history of the simple colon ulcer may be quite variable. On one hand there may be an acute process with rapid perforation leading to a surgical emergency. In this situation the diagnosis is frequently ruptured appendix or rupture of a diverticulum in a patient with left-sided symptoms which may resemble diverticulitis. In other instances, such as the cases reported here, chronicity and recurrence of symptoms may be present. The radiographic diagnosis has been uncertain in many instances because of irritability

associated with inflammatory reaction which prevents adequate filling of the colon in the area of disease. This is sometimes compounded by difficulty in obtaining satisfactory preparatory cleansing of the bowel. In our first case, the diagnosis was made by following the barium through the small bowel into the colon, when it could not be made on barium enema examination.

Etiologic Speculations

The etiology is unknown. Much speculation without supportive evidence is found in the literature. Usual infectious organisms have not been found and there has been no histologic evidence of local vasculitis or generalized vascular disease in the patients reported. Our first case affords some interesting speculation as to a possible viral etiology. Among the cutaneous manifestations of incontinentia pigmenti which the first patient displayed were herpetiform ulcerations of the mouth, lips, and labia. Significantly, these also were of a chronic and recurrent nature. Geneticists would like to postulate a hereditary susceptibility to a *herpes-like virus* in this disease. The relationship of these external ulcers to those of the colon, while remote, makes a viral pathogenesis plausible. This nonspecific type of ulceration also appears to be distinct from the *stercoral** ulcer which occurs in elderly or debilitated patients secondary to adherent inspissated feces and found predominantly in the sigmoid colon.

While the *stercoral ulcer* is considered to be a different clinical entity, the mechanism of colonic stasis from any of a variety of causes is undoubtedly a contributing factor in some instances of nonspecific ulcer. Ulceration proximal to obstructing carcinoma has been noted by Glotzer et al.¹¹ who reported six cases. Multiple ulcers were present in all instances. Some of these had sharply margined ulcers with intervening mucosa intact, while others had involvement resembling idiopathic ulcerative colitis with pseudopolyps. These authors also demonstrated colonic ulceration and inflammation in dogs with experimental obstruction.

Severe nonspecific colitis and enterocolitis have been reported in patients with the functional obstruction found in *aganglionic megacolon* also. The cause is not known, although the ulcers in these cases are evidently related to obstruction.

Interference with mucosal blood supply has also been suggested as a possible cause. These lesions differ from the ulcers of ulcerative colitis in that there is less inflammatory reaction in the former. They differ from the simple ulcers described here in that multiplicity is the rule and inflammatory



Fig. 3-a — Barium enema shows pronounced deformity of the cecum. The remainder of the colon is normal.



Fig. 3-b — Compression spot film of the cecum shows the elongated irregular deep ulcer (long arrow) with the surrounding swollen mucosa and thickened bowel wall which resembles an intraluminal mass. The terminal ileum (short arrow) is slightly compressed but is not otherwise involved.

*See Test Your Word Score Page 1359.

reaction is minimal in these patients with megacolon.

The treatment is surgical excision. There is some difference of opinion as to the extent of excision, particularly in the lesions of the right colon. Surgical removal has generally been successful, but attempts at more conservative management have not. Cases in which long-term follow-up has been available following surgery have shown good recovery. Acute perforation requires emergency surgery with the type of surgery depending on the site of the lesion and the condition of the patient.

Summary

The roentgenographic findings in nonspecific

ulcer of the colon are similar to those of ulcers elsewhere in the gastrointestinal tract. Deformity caused by fibrosis may be extensive. In the chronic or recurrent ulcer, the diagnosis can be made on adequate barium studies of the colon with visualization of the crater. Complete recovery can be anticipated in a high percentage of patients following adequate surgical resection of the lesions. Two cases of nonspecific ulcer of the colon have been presented.

Acknowledgment

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References

1. Bombi, G.: Un Caso di Ulcera Semplice del Cieco. *Policlinico (Sez. Prat.)* 36:1550, 1929.
2. Cruveilhier, J.: *Anatomie Pathologique: Maladies des Intestins.* J. B. Bailliere, Paris, 1835.
3. Barron, M. E.: Simple Non-Specific Ulcer of the Colon. *Arch Surg* 17:355, 1928.
4. Barlow, D.: Simple Ulcers of the Cecum, Colon and Rectum. *Brit J Surg* 28:575, 1941.
5. Wilke, D.: Simple Ulcer of the Ascending Colon and its Complications. *Surgery* 1:655, 1937.
6. Harrison, H.: Importance of Simple Ulcer of the Right Side of the Colon in Diagnosis of Abdominal Disease. *Arch Surg* 40:959, 1940.
7. Cameron, J. R.: Simple Non-Specific Ulcer of the Cecum. *Brit J Surg* 26:526, 1939.
8. Moore, T.: Simple Non-Specific Ulcer of the Ascending Colon. *Brit J Surg* 27:600, 1940.
9. Rosser, C.: Simple Penetrating Ulcer of the Cecum. *Ann Surg* 119:377, 1944.
10. Feldman, M.: *Clinical Roentgenology of the Digestive Tract.* Williams & Wilkins Co., Baltimore, 1948.
11. Glotzer, D. J., Roth, S. I. and Welch, C. E.: Ulceration Proximal to Colon Carcinoma. *Surgery* 56:950, 1964.

Gordeev's Fluid for Cancer

Some new preparations have been developed by Soviet scientists in the fight against cancer. The most common of these used for skin cancer is "Gordeev's Fluid," named after the scientist who discovered it. The liquid is injected by a specially constructed syringe into the substance of the cancer itself and around it, up to the border of the cancer tissue with the surrounding healthy cells. It produces an inflammatory process as a result of which the malignant elements of the cancer die and in its place is formed an ordinary scar.

The Leningrad oncologist, Professor Larinov, in collaboration with Professor Nemets, a chemist of the Leningrad Technological Institute, made a preparation they call "Embikhin," which contains the chemical compound, chlorethylamine. In many animal experiments Larinov gave this substance for treatment of serious cancer of the lymphatic system, and the results were good.*

*L. Fridland, M.D.: *The Achievement of Soviet Medicine*, 1961 edited and translated from the Russian by W. Horsley Gantt, M.D.

Hemostasis and Thrombosis*

A
New
Look

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NEAR THE END of his career, Papanicolaou remarked: "... while it may be a great personal satisfaction to make a discovery in the laboratory, we do not save lives in the laboratory. People's lives are saved where people are." Papanicolaou was aware that laboratories help save lives, but he wanted to point out that physicians actually treat the patient.

This is equally true of diagnosis. No matter how the laboratory helps to formulate the diagnosis, it is the patient's physician who makes and interprets the diagnosis and manages the patient. This is illustrated in two fields—hemostasis and thrombosis—both of which have been extensively studied by laboratory methods. Despite the time and effort expended in laboratories, hemostasis and thrombosis still present formidable problems.

The Cardiovascular System

To manage and control bleeding, one must understand the cardiovascular system. It has two important functional units: the heart and the microcirculation. In between are the relatively passive arterial and venous components.

Arterial and Venous Components

Loss of blood from a vein is rarely serious since the blood pressure is low. In the arteries the pressure is high, but the thick muscular walls protect patients from hemorrhage except when large arteries are severed. Then the hemostatic mechanism is inadequate, and the ligature becomes an indispensable stanching agent.

Microcirculation

The microcirculation is the Achilles heel of the vascular system. The arterioles are divested of much of their muscular protective coat and some are exposed; the capillaries can lose blood by leakage or diapedesis.† Clinicians were unable to

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†See Test Your Word Score Page 1359.

approach the microcirculation and its hemostasis until Duke described the bleeding time in 1910. Here was a direct test on the patient without test tubes or other laboratory manipulations that required theorizing to explain. Duke established that the normal bleeding time was about three minutes and, significantly, that it was not prolonged in hemophilia.

Soon after, Minot and Lee and, independently, Von Willebrand discovered a disease in which the bleeding time was prolonged though the clotting time was not abnormal and the platelets were not reduced. Attempts to pinpoint a platelet or coagulation defect in patients with the disease gave equivocal results. But transfused plasma, even plasma from hemophiliacs, corrected the bleeding time. This indicated the lack of a plasma factor other than factor VIII.

Initial Step in Hemostasis

Effect of Acetylsalicylic Acid

Acetylsalicylic acid prolongs the bleeding time in many normal subjects and in patients with the Minot-Von Willebrand syndrome,* thus helping to formulate the first step in hemostasis (Figure 1). That sodium salicylate lacks this power to prolong the bleeding time gives a clue to how acetylsalicylic acid acts. Obviously, the acetyl linkage, not the salicylic acid, causes the prolonged bleeding time.

Under normal circumstances, a balance of two hormones of the autonomic nervous system, epinephrine—a vasopressor, and acetylcholine—a vasodilator, maintain the tone of the microcircula-

tion (Figure 1). After injury, cholinesterase is activated. Then it hydrolyzes acetylcholine, thereby destroying its vasodilating action. As a result, epinephrine dominates, vasoconstriction ensues, and the first step in hemostasis is completed.

Insufficient Cholinesterase

In a severe case of Minot-Von Willebrand syndrome, insufficient cholinesterase is generated after injury to hydrolyze acetylcholine. Patients bleed because vessels do not constrict initially. In mild or subclinical cases, enough cholinesterase is produced to give a normal bleeding time. But when patients ingest acetylsalicylic acid, the bleeding time becomes longer. The cholinesterase generated combines with the acetylsalicylic acid so that injury does not produce normal hydrolysis of acetylcholine.

While this explanation is theoretical, acetylsalicylic acid does prolong the bleeding time, and this action may be due to the failure of vessels to constrict. In the initial contractile phase, platelets accumulate and aggregate within the injured vessel, and then bring about the second phase of hemostasis. Through their content of serotonin, a vasoconstrictor, they supplement and prolong contraction. By aggregating, they may serve as a mechanical plug, but, more importantly, they liberate a clotting factor which interacts with factors VIII and IX, agents lacking in hemophilias A and B, to produce intrinsic thromboplastin. This substance initiates the clotting reaction which terminates by generating thrombin and forming a fibrin clot which seals the severed vessel and begins the reparative process.

A Three-Prong Mechanism

Hemostasis is essentially a three-phase mechanism, but each phase overlaps the other (Figure 2). They not only complement each other but actually compensate for one another. For instance, the Minot-Von Willebrand syndrome is a mild disorder because other coagulation mechanisms and platelets make up for its defect.

This protection against blood loss can be visualized as a three-line defense. Blood coagulation constitutes the third line of defense. Even with hemophilia, hemostasis is surprisingly good. Many hemophiliacs do not bleed from minor cuts, do not have nose bleeds, and do not experience gastrointestinal bleeding because the first line of defense, as measured by the bleeding time, is

*See Pages 1338 and 1423.

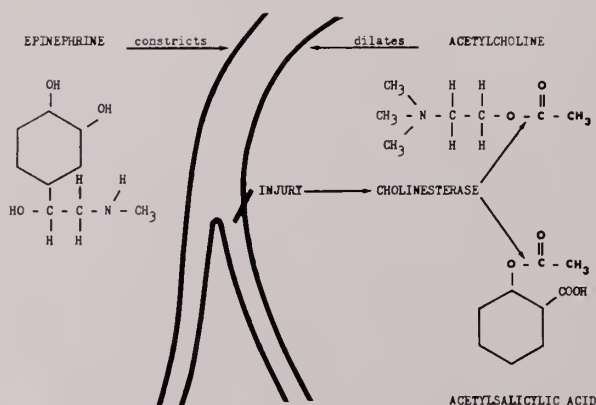


Fig. 1—Acetylsalicylic acid as a probable competitor of acetylcholine for cholinesterase.

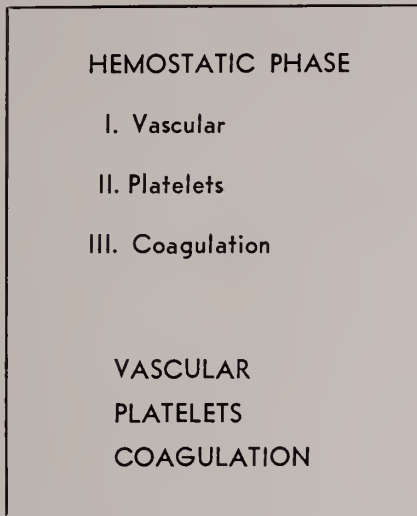


Fig. 2 — The 3-line hemostatic defense.

normal.

Diagnosis of Hemorrhagic States

The three-phase scheme of hemostasis outlines the disorders and diagnostic tests for hemorrhagic states (Table). The bleeding time and the aspirin tolerance test, a bleeding time after a test dose of acetylsalicylic acid, identify the Minot-Von Willebrand syndrome. With the prothrombin consumption time, a platelet dysfunction can readily and reliably be established. In patients the qualitative platelet defect or thrombopathy is equally as important as thrombocytopenia. The one-stage prothrombin time and the prothrombin consumption time screen coagulation defects.

Fortunately, the wide use of the prothrombin time to control oral anticoagulant therapy has

made this procedure routine in most hospitals. The prothrombin consumption time is equally simple. A technologist who knows how to do the prothrombin time needs no additional training for this test. With minor modifications the prothrombin time and the prothrombin consumption time can sensitively detect nearly all coagulation defects.²

Common Types of Hemorrhage

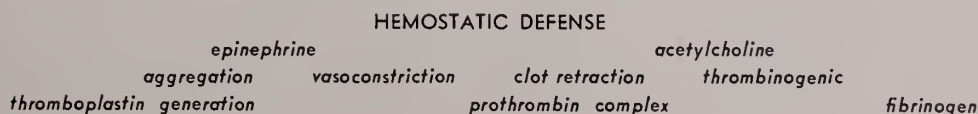
Today those who write about hemostasis emphasize coagulation reactions and platelets. This is evidenced by a stream of papers on clotting factors, fibrinolysis, platelet stickiness, and platelet agglutination. Prosaic types of bleeding such as epistaxis, occult gastrointestinal bleeding, and menorrhagia receive scant attention. If the bleeding is sufficiently severe, patients may be sent to a specialist who handles the bleeding empirically.

Yet, these three types of hemorrhage outnumber all other forms of bleeding and bedevil the practicing physician. Each always has an underlying cause, and the physician's responsibility is to find it.

To do this, a medical history including hereditary background and a physical examination must precede the laboratory studies. The prothrombin time and the prothrombin consumption time will reliably screen coagulation and platelet defects. In most patients, neither a coagulation nor a platelet defect will be found. But since the Minot-Von Willebrand syndrome is the most common bleeding disease and is responsible for much mucous membrane bleeding, a surprisingly large number of cases will be detected by the aspirin

TABLE
A Diagnostic Guide to Hemostasis

DIAGNOSTIC TESTS	RESULTING HEREDITARY DISORDERS
Duke bleeding time	Minot-Von Willebrand syndrome
Aspirin tolerance test	
Prothrombin consumption time	Thrombocytopenias
Thromboplastin generation test	Thrombopathies
Clot retraction	
Platelet count	
Clotting time	Afibrinogenemia
Prothrombin time	Hypoprothrombinemia
Prothrombin consumption time	Deficiency of factor V, VII, VIII, IX or X
Thromboplastin generation test	Hyperheparinemia



tolerance test.

The Minot-Von Willebrand syndrome, however, does not explain all mucous membrane bleeding. Epistaxis, for example, is more troublesome in hereditary telangiectasia.* Other disease can cause gastrointestinal bleeding, and the complex hormonal control of menstruation certainly does not permit singling out one cause to explain all cases of menorrhagia. Yet with the aspirin tolerance test as a screening procedure, Minot-Von Willebrand's disease can often be detected and the correctness of the conclusion verified clinically when patients stop bleeding after being off medications containing acetylsalicylic acid.

Multiple Hemostatic Defects

The first phase of hemostasis is vascular contraction. This is independent of both coagulation and platelets and is responsible for controlling the bleeding from small cuts and minor trauma. Often it is assumed that the bleeding in hemophilia is solely and directly dependent on the plasma concentration of factor VIII. However, I have had the opportunity to follow the clinical course of two hemophilic brothers, both of whom have a concentration of factor VIII of about 0.01 per cent of normal. Yet one of the brothers has required only two hospitalizations for bleeding and has no crippling joint deformities. His older brother has had numerous hospital admissions and is severely crippled. The first has a normal aspirin tolerance test while the second not only has a poor aspirin tolerance but has been a chronic user of this drug. These boys eloquently demonstrate that the severity of the bleeding tendency in hemophilia is not solely dependent on coagulation. By superimposing a faulty initial phase in hemostasis on a basic coagulation defect, the bleeding tendency is strikingly accentuated.

What is true of hemophilia should be equally applicable to other bleeding states. Today thousands of patients have coagulation depressed by oral anticoagulant drugs. Occasionally, serious hemorrhage occurs when the prothrombin time indicates a presumably therapeutic range. How many of such patients could be spared complications of this type by screening with the aspirin tolerance test and the judicious use of this drug, can only be surmised.

Thrombosis

Just as has hemostasis, so has thrombosis been

*See Test Your Word Score Page 1359.

dominated by thinking along the lines of platelet agglutination and hypercoagulability. Yet, in the slaying of the man who shovelled snow on a cold winter morning, it would be difficult for any scientific jury to find either the platelets or the coagulation mechanism guilty of having delivered the blow that stopped the heart. Arterial thrombosis presents a complex problem. Perhaps many of the atheromatous plaques represent scars of previous victories rather than punishment for having eaten Minnesota or Wisconsin butter. While platelets and coagulation do play a role in arterial thrombosis, it is equally certain that the autonomic nervous system with its own hormones along with various other hormones must be integrated to obtain a global concept.

Venous Thrombosis

Arterial thrombosis is too complex for this discussion, but venous thrombosis is not³ (Figure 3).

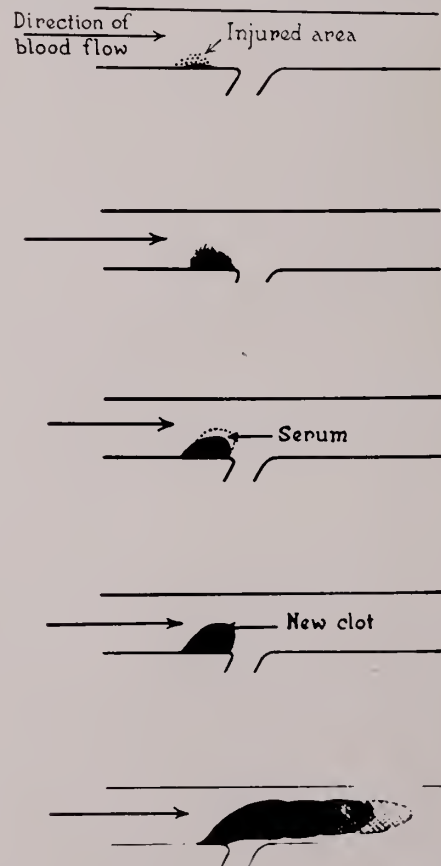


Fig. 3—The probable sequence in the formation of a venous thrombus. The initial injury of the vessel wall serves as the nidus by attracting platelets, with formation of a small clot which propagates by the extrusion of serum rich in thrombin. Sluggish circulation and anemia are controlling factors.

A slight injury to a vessel wall is probably common. Such an injury site attracts platelets which adhere to it, then enter into the clotting mechanism and assist in the generation of a little thrombin which clots enough fibrin to cover the affected area. Whatever excess thrombin is generated either becomes adsorbed to the fibrin matrix or is washed away by the bloodstream. Should the blood flow be sluggish, the local clot would enlarge and then on retraction extrude a serum rich in nascent thrombin. A secondary clot, attached to the primary one, then forms, repeating the cycle of retraction and extrusion of nascent thrombin.

Thus, from a small area on a vessel wall a thrombus can form and become large enough, when it is broken off by fibrinolysis, to produce a fatal pulmonary embolus. In such a concept, hypercoagulability can be dismissed; but hypo-coagulability as induced by anticoagulant drugs may counteract the thrombotic process. Anemia is dangerous because it brings about more rapid and complete clot retraction. On the troika of (1) improved venous circulation, (2) corrected anemia, and (3) effective anticoagulation, the journey towards prevention of venous thrombosis should be more successful.

Summary

Hemostasis is maintained by a three-line de-

fense:

1. Vascular contraction after injury brought about by the autonomic nervous system,
2. Platelets which supplement and complement the primary contraction and which initiate coagulation by supplying a factor essential for the intrinsic generation of thromboplastin, and
3. The coagulation mechanism which brings about the sealing of injured vessels and the beginning of the reparative process.

The important bleeding disease in which the defect is in the first phase is the Minot-Von Willebrand syndrome. The severity of a bleeding tendency is often a combination of defects in at least two components of the hemostatic mechanism.

Phlebothrombosis is dependent on an initial vascular wall injury which may actually be small and insignificant but still serve as the nidus for the growth of a large attached clot under the favorable conditions of sluggish circulation and anemia. This may eventuate in a massive pulmonary embolus. Hypercoagulability which is difficult to define or envision need not be postulated to explain a thrombotic proneness, but the induction of hypocoagulability by anticoagulant therapy has clinical support as a means of reducing venous thrombosis.

References

1. Quick, A. J.: Salicylates and Bleeding: Aspirin Tolerance Test. *Amer J Med Sci* 252:265, 1966.
2. Quick, A. J.: Detection and Diagnosis of Hemorrhagic States. *JAMA* 197:418, 1966.
3. Quick, A. J.: Hemorrhagic Diseases and Thrombosis. Lea & Febiger: Philadelphia, 1966.

Frontier Granny Medicine

Sometimes young frontier doctors were given a few constructive suggestions from old grannies. These varied in their usefulness. Dr. Felix Collard, Wheelock, Texas, met an old lady riding down to the forks of Camp Creek.

"Be you a doctor?" she asked.

"Yes, I'm a practicing physician."

"Do you know a sure cure for pneumonia?"

"I fear I do not."

"Well, you are a young doctor, and I want to help you along and I want to give you a sure-shot cure for pneumonia. It's black cat tail tea. Find the blackest cat that you are able to find and cut off his tail and make a tea and mix it about half and half with good red liquor and have it hot. Give one tablespoonful every ten minutes until the patient goes to sleep. The only times I've known it to fail was when the cat wasn't black enough, the tail wasn't long enough or the patient didn't get the cure soon enough."*

*Richard Dunlop, M.D.: Doctors of the American Frontier.

President's Letter

Continued from Page 1309.

the time you spend golfing or vacationing. Couldn't you spare 10 hours a quarter for some kind of political endeavor? And how about your wife? She has much more leisure time than you and should respond graciously and willingly to donate some of that time to political activities.

What is your community leadership score?
What is your wife doing with her spare time?



C. G. Sheppard, M.D.
President

Minnesota State Medical Association

Von Willebrand - Jürgens Syndrome

This has been classified as a constitutional, non-malignant, hereditary, hemorrhagic diathesis. Inheritance is as a simple mendelian dominant and numerous family members may be involved, usually in childhood.

Epistaxis occurs from nasal mucous membrane gingivae and from gastrointestinal or renal sources. There may be hemorrhages in the retina or in cutaneous tissue as petechiae with spontaneous ecchymosis. The platelet count is normal, but bleeding time is prolonged.*

*See page 1334.

Durham, Robert H.—Encyclopedia of Medical Syndromes
Hoeber Medical Division, Harper and Row, New York

MINNESOTA MEDICINE Cover Photographs

In order to encourage more physicians to submit color slides for use on the cover of MINNESOTA MEDICINE the competition is being discontinued. The picture editor now invites all physician-photographers to send 35 mm. color slides of suitable subjects for consideration as cover pictures. The format must be horizontal because of printing limitations. Pictures highlighting Minnesota seasons, places, and activities will have an automatic advantage. No limit as to the number of slides sent will be set, but all slides should be individually identified. All slides will be returned. Physicians whose pictures are used as covers will be recognized in MINNESOTA MEDICINE. We can use many more pictures than we have received in the past.

Music and Disease

And it came to pass, when the evil spirit from God was upon Saul, that David took an harp, and played with his hand: so Saul was refreshed, and was well, and the evil spirit departed from him.

—I Samuel 17, 23.

Angiosarcoma of Lungs and Adrenal Gland

Unusual Clinical and Pathologic Manifestations

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REGINALD H. SMART, M.D.*
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MALIGNANT VASCULAR tumors are rare, and if they occur primarily in internal organs, the clinical diagnosis may present problems.^{1,6,9} Approximately two thirds of malignant vascular tumors are classified as Kaposi's sarcoma.² The great majority of patients with this disease have lesions on one or both lower extremities, but visceral lesions may be present,^{11,5,7,8} and occasional cases in which lesions histologically characteristic of Kaposi's sarcoma were limited to viscera have been recorded.^{1,5,8} The lungs are frequently involved by metastatic disease^{11,12,13} but primary involvement of the lungs by angiosarcoma or Kaposi's sarcoma is extremely rare.^{4,1} No reference could be found in the literature to primary involvement of the adrenal gland.¹⁶

The case presented is that of a patient who had an angiosarcoma involving his left adrenal and associated multifocal involvement of the lungs.

Case Report

The patient was a 57-year-old Jewish man with a two-month history of hemoptysis when first admitted to the hospital on September 23, 1965. Roentgenologic examination prior to admission had demonstrated a mass in the right upper lobe, and bronchoscopy showed bleeding from the right upper-lobe bronchus. After bronchoscopy the patient noted shortness of breath and a slight cough. The past history was unremarkable. He had smoked two packs of cigarettes daily until two years before. The physical examination at admission showed a blood pressure of 142/90. The hemoglobin measured 12.7 Gm. per 100 ml. of blood, with a leukocyte count of 8,100 per cubic millimeter and a normal differential count. On September 24, a right upper lobectomy was performed because of a presumptive diagnosis of bronchogenic carcinoma.

Operative Findings

The resected right upper lobe was pinkish-red, and the apical region and large portions of the posterior and anterior segments were atelectatic, hyperemic and hemorrhagic. There was no gross evidence of neoplasia, thrombi or emboli. Microscopic examination showed massive intra-alveolar hemorrhage and adjacent alveoli were found to contain a fibrinous exudate with associated active histiocytic and fibroblastic proliferation

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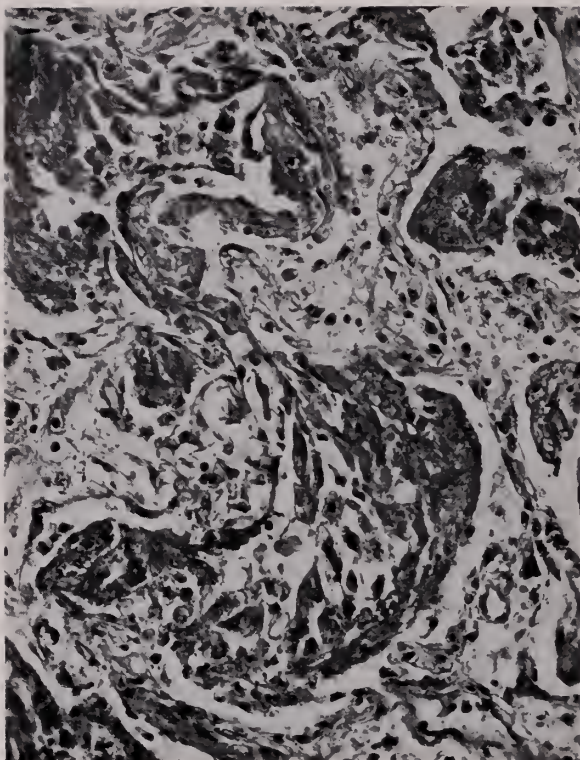


Fig. 1—Organizing infarct in resected right upper lobe (X 250).

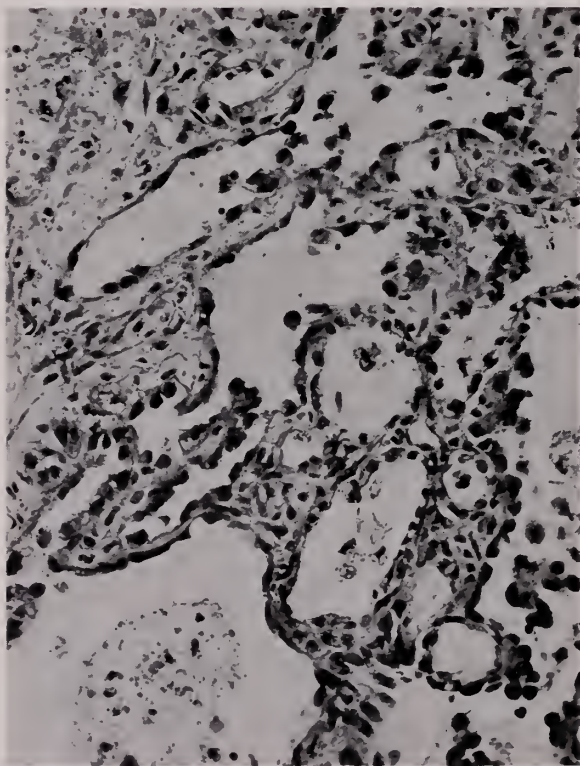


Fig. 2—Lung biopsy. Note alveolar spaces lined by neoplastic endothelial cells (X 250).

(Figure 1). Neoplasia or vascular proliferation was absent. Despite the absence of demonstrable vascular lesions, the intrapulmonary hemorrhage with localized organization was considered to represent infarction.

Postoperative Course

The postoperative course was uneventful and the patient was discharged on October 3. Serial A-P full-chest planograms revealed multiple nodules measuring 0.5 to 2.5 cm. distributed throughout both lungs, as well as bilateral mediastinal adenopathy. The findings were considered to be those of a disseminated hematogenous disease. Laboratory examination showed moderate anemia, with a hematocrit value of 29%, and a leukocyte count of 9,200; other tests were within normal limits. Biopsy of a left scalene lymph node failed to demonstrate significant abnormalities.

Subsequent Operative Findings

On October 18, a left thoracotomy was performed and several nodular lesions that measured from 2 to 20 mm. in diameter, located in various portions of the left lung, were biopsied. The tissue was yellowish to pink-red, nodular and moderately firm. Microscopically, there were multiple areas of necrosis and recent hemorrhage with focal organization and focal zones of greatly atypical cellular proliferation, occasionally with a papillary pattern. Some of these proliferating atypical cells were clearly alveolar in origin, but others could not be clearly identified as to type and site of origin (Figure 2). The findings were interpreted as a continuing process of

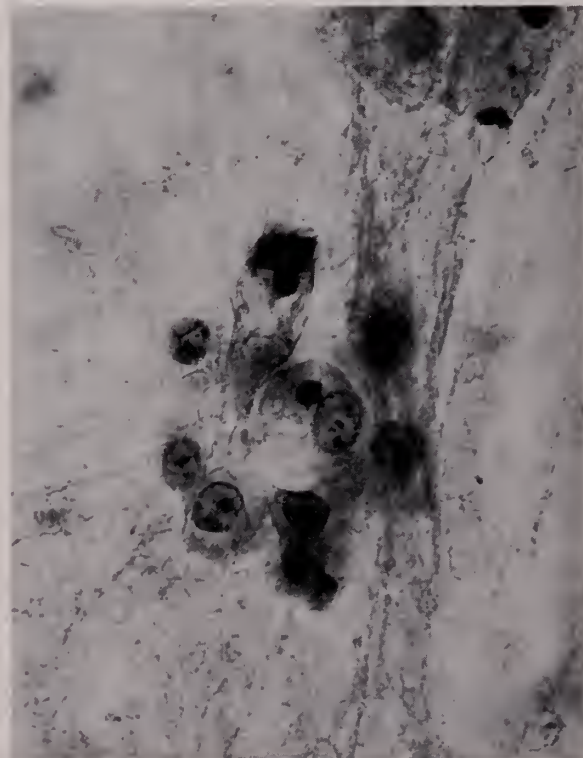


Fig. 3—Sputum showing single most atypical cluster in multiple specimens. Note histiocytes or neoplastic endothelial cells (X 850).

thromboembolism with pulmonary infarcts of varying age, inducing a very atypical bronchiolar hyperplasia suggesting the possibility of Kaposi's sarcoma.

Repeated cytologic examination of the sputum demonstrated only atypical histiocytes (Figure 3). Biopsy of a subcutaneous nodule in the neck on January 3, 1966, showed necrotizing inflammation and acute focal vasculitis, with occasional bizarre cells in necrotic areas similar to those observed in the lung biopsy.

After the thoracotomy, the patient grew progressively more weak and dyspneic. Values for hemoglobin and hematocrit remained low and he required repeated transfusions. Because of the possibility of pulmonary infarctions, as suggested at biopsy, the inferior vena cava had been ligated on October 22, 1965. At that time, all intestinal organs were normal to inspection and palpation, with the exception of the esophageal hiatus, which admitted three fingers. After the caval ligation, the legs became edematous. The patient continued to have hemoptysis, with fever up to 101°F. Because of the possibility of a collagen disease, such as Wegener's granulomatosis, he was given prednisolone and antibiotics. His condition continued to deteriorate and he died on January 6, 1966.

Autopsy Findings

The body showed no palpable peripheral lymphadenopathy or cutaneous lesions. Small, cystic, dark-red, nodular, hemorrhagic lesions averaging 5 mm. in diameter were noted in the anterior mediastinum, and larger confluent hemorrhagic nodules were seen in the parietal epicardium. The lung tissue was consolidated, dark reddish-pink, and contained yellowish to dark-red areas of old infarction, as well as several hemorrhagic nodules measuring up to 3 cm. in diameter. Most of these nodules were lobulated and located peripherally, with smaller hemorrhagic nodules in the pleura. Several peribronchial lymph nodes were enlarged to a diameter of 4 cm. and were soft, dark-red and hemorrhagic. Mediastinal lymph nodes showed similar changes. The gastrointestinal tract showed several small, raised, dark-red hemorrhagic mucosal nodules 5 mm. in diameter; one of these nodules was in the esophagus just above the cardia, four were in the stomach, and several were scattered throughout the mucosa of the jejunum. Similar 2 to 5 mm. hemorrhagic nodules were found in the subcapsular hepatic parenchyma, and a small nodule was present in the mucosa of the gallbladder. The right adrenal was of normal size and shape. The left adrenal was largely replaced by a mottled, yellowish to dark-red, hemorrhagic, soft, friable mass measuring 7.5 by 6 by 5 cm. In several places the thinned

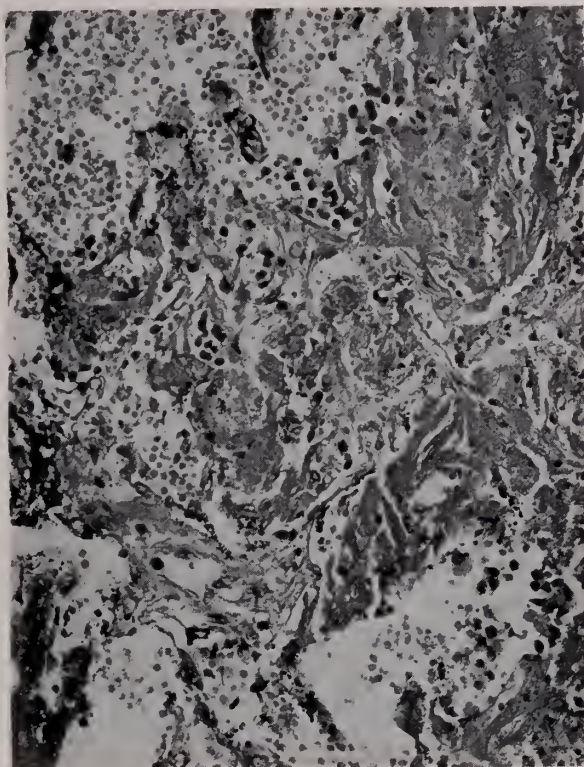


Fig. 4—Lung at autopsy showing infarct-type necrosis with organization, resembling infarct in resected lobe (X 250).



Fig. 5—Direct smear of lung nodule at autopsy (Papaniicolaou stain X 850).

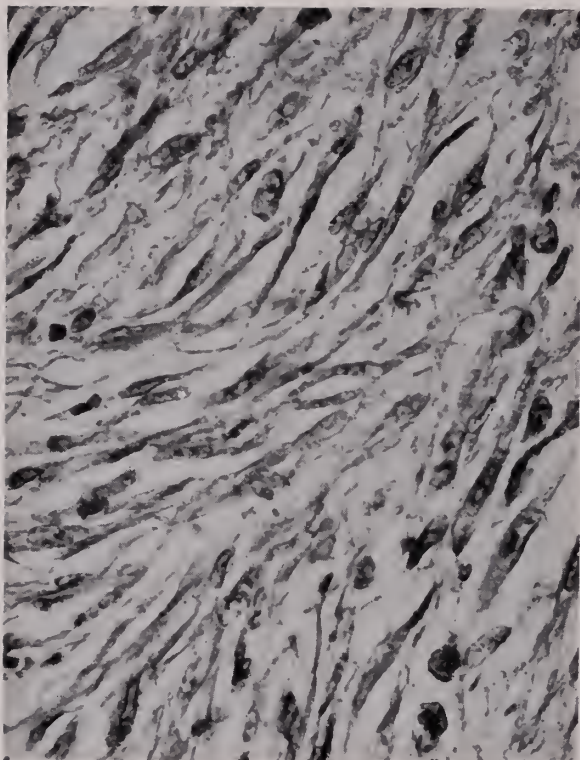


Fig. 6—Tumor in left adrenal showing spindle-cell (fibrosarcoma-like) component (X 500).

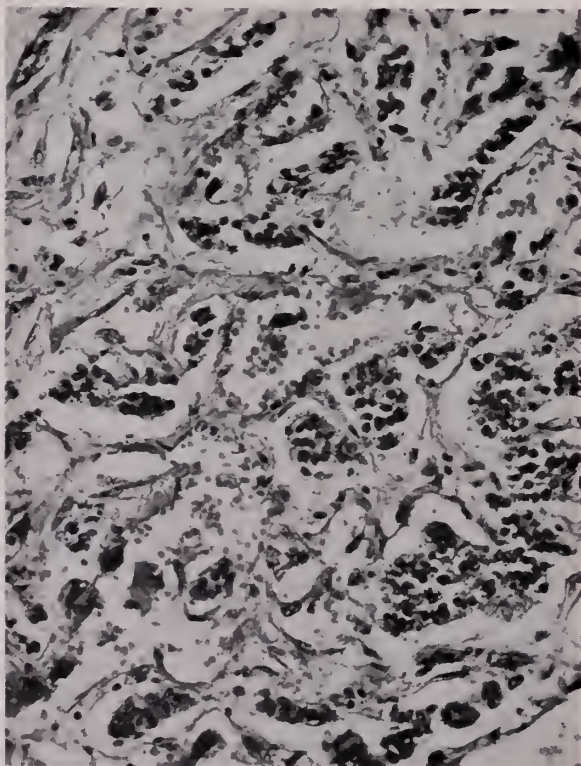


Fig. 7—Tumor in left adrenal gland demonstrating vascular spaces in cortex overlying main tumor (X 250).

adrenal cortex was stretched over this hemorrhagic tumor, which appeared to be of adrenal origin. A few small hemorrhagic nodules were also seen in the vertebrae.

Sections of the lungs showed multiple areas of consolidation and hemorrhage measuring from 0.8 to 3.5 cm. in diameter, located generally in the periphery. In the lower lobe of the left lung they were associated with acute necrotizing pneumonitis and severe polymorphonuclear leukocytic infiltration, whereas the lesions in the upper lobes were more hemorrhagic and resembled infarcts (Figure 4). Many of the alveolar septa either were necrotic, or were lined by cuboidal alveolar cells or neoplastic, apparently endothelial, cells. Smears showed the cytologic atypical proliferation to be considerably greater than that observed in the sputum (Figure 5).

In one area in the lower lobe, essentially normal alveolar lining could be traced, gradually changing to cells with larger nuclei that were elongated and resembled endothelial cells, and finally to a termination as a papillary club-shaped cluster formed and covered by neoplastic cells. The enlarged peribronchial lymph nodes showed extensive hemorrhage with a residual rim of lymphoid tissue measuring 2 mm. in thickness.

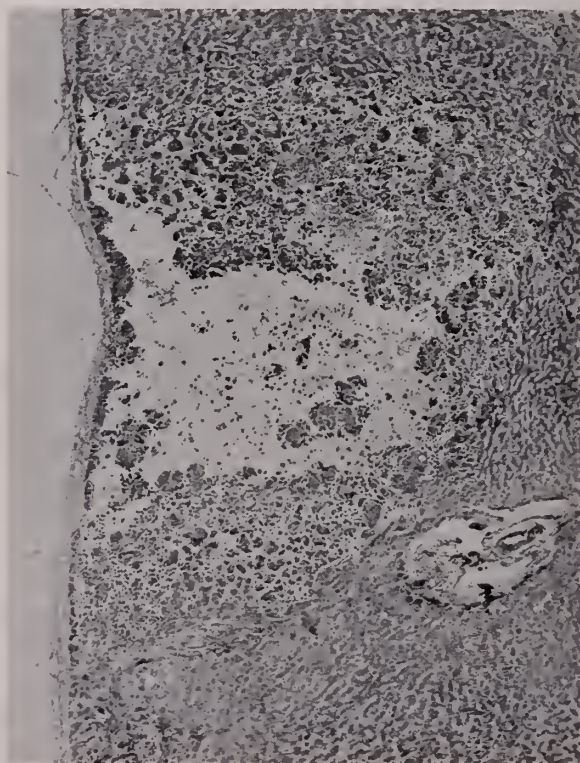


Fig. 8—Vascular subcapsular tumor in liver (X 40).

The mass in the left adrenal consisted mainly of proliferating, neoplastic, spindle-shaped cells with fairly large, generally elongated, hyperchromatic nuclei and a moderate amount of cytoplasm (Figure 6). Neoplastic vascular spaces were prominent (Figure 7). Residual adrenal cortex covered portions of the tumor, indicating direct involvement of the adrenal. The small nodules in the intestinal mucosa and liver demonstrated hemorrhage and proliferation of endothelial-like neoplastic cells partially forming vascular channels (Figure 8).

Comment

This case presents a number of unique and interesting pathologic features. It is debatable as to whether the lesion should be classified as a visceral form of Kaposi's sarcoma or as an angiosarcoma, presumably arising primarily in the left adrenal. Since the cutaneous lesions found in the vast majority of cases of Kaposi's sarcoma¹¹ were lacking and since histologically the tumor lacked the characteristic spindle-cell proliferation surrounding open vascular-like slits devoid of endothelial lining,⁵ a classification as angiosarcoma appears preferable. The fibrosarcoma-like spindle-cell proliferation seen mainly in the adrenal tumor may occur in angiosarcoma as well as in most other sarcomas.⁷ Primary angiosarcoma of the adrenal or predominant adrenal involvement in Kaposi's sarcoma has not been recorded in the literature.

The atypical proliferation of pulmonary alveolar cells is of special interest.^{14,15} These changes are particularly evident in infarcts or in pulmon-

ary fibrosis and may precede the development of adenocarcinoma of the lung.^{14,16} In our case there was pronounced and atypical alveolar-cell hyperplasia that was more prominent in the biopsy specimen than in the autopsy material, perhaps due to modification by treatment with corticosteroids. The alveolar-cell proliferation appeared to merge with and in a few areas could be traced to neoplastic proliferation of an angiosarcomatous rather than a carcinomatous lesion. The pattern suggested that the tumor in the lungs represented a multifocal process rather than a metastatic one and that the alveolar lining cells were undergoing in-situ malignant changes. A similar observation was made by Loring and Wolman¹ in their case of Kaposi's sarcoma of the lungs. They also noted the bizarre reaction of alveolar lining cells in contact with tumor, stating that the structural aberrations satisfied many of the histopathologic criteria for the diagnosis of malignancy. However, they thought that the absence of significant cellular proliferation or evidence of invasion suggested that the appearance of anaplasia was not associated with capability for autonomous growth.

Summary

The case of a 57-year-old man with angiosarcoma of the left adrenal and extensive metastatic or simultaneous multifocal involvement of the lungs is reported. Hemoptysis was the first symptom, and the original pathologic diagnosis was that of pulmonary infarction. The unique pathologic features and the changes in pulmonary alveolar cells associated with the neoplastic process are demonstrated.

References

1. Loring, W. E. and Wolman, S. R.: Idiopathic Multiple Hemorrhagic Sarcoma of Lung (Kaposi's Sarcoma). New York J Med 65:668, 1965.
2. McCarthy, W. D. and Pack, G. T.: Malignant Blood Vessel Tumors. Surg Gynec Obstet 91:465, 1950.
3. Hall, E. M.: A Malignant Hemangioma of the Lung with Multiple Metastases. Amer J Path 11:343-353, 1934.
4. Spencer, H.: Pathology of the Lung. MacMillan Company, New York, 1962.
5. Anthony, C. W. and Koneman, E. W.: Visceral Kaposi's Sarcoma. Arch Path 70:740-746, 1960.
6. Bourne, M. S., Cook, T. A., and Williams, G.: Hemangiosarcomatosis: Two Cases Presenting as Hematological Problems. Brit Med J 5456:275, 1965.
7. Landing, B. H. and Farber, S.: Tumors of the Cardiovascular System. Armed Forces Institute of Pathology, Washington, D. C., 1956.
8. Tedeschi, C. G., Folsom, H. F., and Carnicelli, T. J.: Visceral Kaposi's Disease. Arch Path 43:335, 1947.
9. Lukash, W. M., Schneider, P. J. and Semmett, C. O.: Angiosarcoma Presenting as Acute Rheumatic Pancarditis. JAMA 193:975, 1965.
10. Stout, A. P.: Tumors of the Soft Tissues. Amer Reg Path AFIP Washington, D. C., 1953.
11. Reynolds, W. A., Winkelmann, R. K. and Soule, E. H.: Kaposi's Sarcoma: A Clinicopathologic Study with Particular Reference to Its Relationship to the Reticuloendothelial System. Medicine 44:419, 1965.
- 12-16. May be secured from the author or the reprints.

No man has ever yet discovered the way to give friendly advice to any woman, not even to his own wife.—Balzac

Intensive Care Unit*

"I C U" said a nurse beside my bed.

Groggily, I thought she was playing "Peek-a-boo" with me and I replied, "I see you too, cutie." She had merely answered a question put to her by someone beyond my hearing. I was in the INTENSIVE CARE UNIT.

The last thing I remember prior to that was being laid out on a pad under a battery of light reflectors and being pleasantly told that I would be put to sleep.

What a vast difference there is in being anesthetized today compared with years ago in the days of chloroform and ether. I well remember the gagging sensation and the whirling brain that accompanied the first whiff of ether and the violent retching afterward.

From Wednesday through Saturday in the Intensive Care Unit I can recount little that is cogent. Much of the time must have been spent in the twilight zone, because the greater part of what I recall of those days and nights makes very little sense. I do remember the monotonous frequency of the thermometer, the blood pressure and pulse count around the clock; and I recall the angels of mercy with their hypods. At the least unusual sound two nurses were instantly at my side, where the head of my bed was equipped with every modern facility for saving life in an emergency.

Uppermost in my semi-comatose mind was that my surgeon and his consultants had emphasized that at all costs I had to cough—and cough some more. One strong young Nightingale invariably came and held me in her bear-hug, easing the pain immeasurably. She was warm and strong and fragrant, and she made this old man feel that he was important. I hated to be coughing almost directly in her face, but she said that it made no difference, that my cough was my own saving grace, as I had developed an atelectasis.

I made frequent trips in and out of the twilight zone during these five days and nights, and I talked audibly to people I have neither seen nor heard from in half a century and know not whether they are living or dead. At one point the Intensive Care Unit became a quonset hut in Achiet-le-Grande back in 1916 where the Canadian Corps on the Somme had its casualty clearing station and where a train-load of wounded soldiers had just been brought in. No life-saving

antibiotics in those days: either you had the Lord on your side or you passed in your checks: a dichotomy that made you a confirmed fatalist. Then back to reality and the unfinished job at hand—to cough, and cough some more.

When I was not sleeping, hour after hour was engrossed in watching the myriad holes in the acoustic ceiling tile as they transformed themselves into the most delicate gossamer lace, which constantly and gently rolled down in billowing folds until I could reach my hand up to penetrate its depths. I could not feel the lace; yet it was there. Was this, indeed, a shroud of the twilight zone stealthily seeking to envelop me on a trip to eternity? No, there were things left undone on earth—so cough, brother, cough. The coughing racked me with pain, but it set the ceiling back to normal so that the holes in the tile reappeared. But then I relapsed into my drugged and fevered semi-consciousness with the gossamer lace again re-forming and the cycle commencing all over again. I did not panic but simply waited until that shroud had almost reenveloped me before I beat the powers of fate by again coughing.

On several occasions the seemingly inexorable approach of the lace curtain was attacked by a force of millions of little black bugs that darted in and out as if attempting to repulse it. The lace and the bugs see-sawed back and forth for supremacy—the lace eventually winning out and swallowing up its attackers as it continued its relentless urge of smothering me in its folds. Needless to say how pleased I was on the first day out of Intensive Care when I had full control of all my senses and could receive visitors!

I shall always sing hymns of praise for the unselfish dedication of the Nursing Staff of the St. Barnabas Hospital Intensive Care Unit, not only for the attention that they paid to me, but that which was given to the others in the Unit. The nurses are all, indeed, true Florence Nightingales and have a right to be proud of their profession.

I do not wish to imply that no credit is due to my surgeon and his consultant and all of the others who helped in my recovery, for it is their knowledge and experience and dexterity that have made an Intensive Care Unit an efficient and invaluable adjunct of a modern hospital.

Albert (Ray) Plantan
Brainerd, Minn.

*Excerpts from a letter.

Diabetes, Peptic Ulcers, and the Hypothalamus

ROBERT E. BUCKLEY, M.D.
San Francisco, California

IT HAS LONG been known by clinicians that there is an apparent protection against the development of peptic ulcers among patients who have diabetes. The incidence of peptic ulcers among diabetics is about one fourth that of the general population. In 1940 Wilder reported that 3.5 per cent of the general population develop ulcers, but only 0.77 per cent of diabetic patients do. No cases of peptic ulcer were reported in a group of 4,103 diabetic patients before insulin.¹ One of the important effects of the treatment of peptic ulcers with the Sippy diet is that the frequent feedings induce a consistent hyperglycemia.

Hypoglycemia

There is an increased occurrence of hypoglycemic reactions among patients who have peptic ulcers. Berry found that seven of 10 of his ulcer patients had functional hyperinsulinism during their five-hour glucose tolerance test when the test was taken without dietary preparation.² None of his 10 control patients developed hypoglycemia. Abrahamson found that all members of a group of twenty-seven ulcer patients developed hypoglycemia.³ Hypoglycemia has been found to increase the gastric acidity, cause hypersecretion, increase peristalsis, and induce hypertonus.² Studies of the effect of hypoglycemia on experimental animals confirm these clinical findings. Poth and From reported that 50 per cent of dogs sustained in hypoglycemia would develop ulcers.⁴ The studies by Hans Selye on the gastrointestinal tract responses in the alarm reaction are quite pertinent here. In 1936 he reported that insulin overdosage, like other procedures which cause hypoglycemia—such as adrenalectomy, fasting, and partial hepatectomy, will increase the incidence of ulceration when other stresses are applied to rats.⁵ He reported a further study in 1944 which has even more importance to the study of the relationship of blood sugar and peptic ulceration. He found that various foods, and particularly dextrose, were effective in protecting animals from ulcers,⁶ and that dextrose gave protection when given by gastric lavage and also when given parenterally. In this study, the stresses which

were applied to the rats, such as pain, cold, and transection of the spinal cord, did not induce hypoglycemia. The implication of this study by Selye is that hyperglycemia has a protecting effect over and above that of merely preventing hypoglycemia.

The biologic basis of these findings will be found in the more recent work which has been done on the neurophysiology of the hypothalamus. Two study groups have focused attention on the hypothalamus: the neurophysiologists concerned with the central nervous system's influence on the gastrointestinal tract,⁷ and the nutrition groups concerned with appetite and the gluco-receptor centers within the hypothalamus. When the work of these investigators is combined, the biologic basis for these observations is clarified.

The groups which are concerned with the influence of the central nervous system on gastrointestinal tract activity usually separate the hypothalamus into the anterior and posterior sections. The anterior area has been described as having a rather basic association with the parasympathetic division of the autonomic system. Stimulation in the anterior area is associated with increased activity of the gastrointestinal tract, including increased secretion of hydrochloric acid. These effects are mediated by way of the vagus nerve.⁸ Stimulation here has also caused thickening of the gastric mucosa, with changes in its

cell types and distribution which are consistent with the increased gastric acidity and the peptic ulcers which develop.⁹ Destructive lesions in the posterior portions of the hypothalamus have been reported to have similar effects of inducing both gastric hemorrhages and ulcers. The similarity of results of anterior stimulation and posterior destruction are believed to result from the over-activity of the anterior portions occurring in both instances. The anterior hypothalamus can become more active when deprived of its interaction with the posterior region which is necessary for over-all balance of function.

There has also been some similarity of results when destructive lesions of the anterior regions are compared with stimulation in the posterior regions. These experiments have caused the development of hemorrhages, and perhaps gastromalacia, but have not been associated with the development of peptic ulcers.¹⁰

One problem of these experiments needs to be considered here. There is no clearly demarked or definable line of separation of the anterior and posterior areas. The conclusions of Long in 1962 was that it is most important to get electrode placement in "a low, mid-line position" in order to cause the non-specific autonomic dysfunction which he felt was basic for disturbance of function of the gastrointestinal tract.¹¹ This study cautions that we should not attempt to be too precise or rigid in our designation of anterior or posterior areas; it emphasizes that the consistent responses which have been obtained by many different investigators have come from the areas which border upon the lower part of the third ventricle.

The nutrition groups have focused their attention on the medial and lateral hypothalamic areas. The medial area, containing the ventromedial nucleus, functions as a "satiety area" to inhibit activity in the "feeding area" of the lateral hypothalamus.¹² The medial satiety area has been found to be sensitive to the level of circulating glucose. Elevations of blood sugar will cause the satiety area to inhibit the lateral "feeding area." Destruction of the ventromedial nucleus will prevent it from inhibiting the feeding area which then becomes overactive. Such animals develop hyperphagia and become obese. Destruction of this lateral "feeding area" causes such food avoidance that the animals may starve themselves if not force-fed.

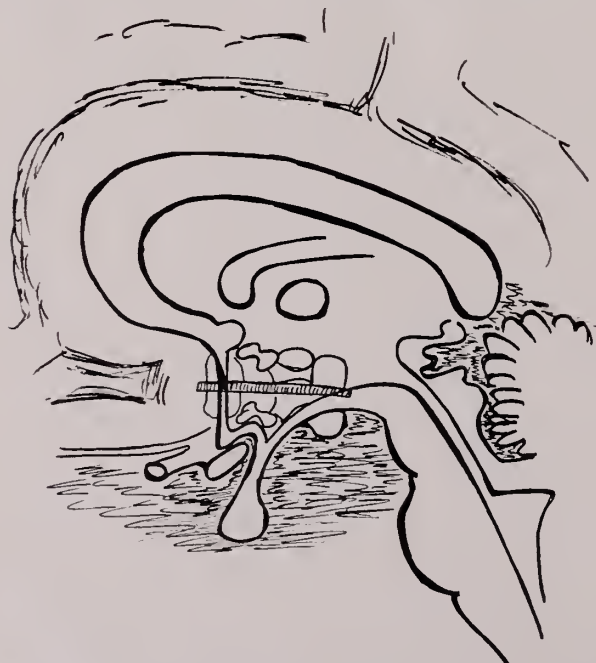


Fig. 1—This section of the brain illustrates the site of the hypothalamus, and indicates the location of the cross-section of the hypothalamus.

Gluco-Receptor Area

It is the presence and location of the gluco-receptor area which is of importance for the topic of peptic ulcers and diabetes. Changes in the levels of activity of these areas have been demonstrated to be associated with the levels of blood glucose.¹³ Another type of demonstration of the locus of sensitivity to sugar has been the destruction of certain areas here by gold thioglucose. When this chemical is given to rats at the LD-50 dosage level, 60 per cent of the survivors will have a pattern of overeating and obesity which is similar to that of animals with stereotaxic lesions of the ventromedial hypothalamic nucleus. The microscopic examination of their brain reveals destruction of neurons of the arcuate or periventricular nucleus, the ventromedial nucleus and occasionally the supraoptic nucleus. These lesions occur only if glucose is part of the molecule, since similar compounds, such as gold thio-glycerol or gold thiomalate, have comparable toxicity yet do not give localized injury here. These chemical lesions help us to identify the glucose-sensitive areas of the brain more precisely, and they are found to be in the low mid-line areas, bordering on the lower part of the third ventricle.

The influence of diabetes on gastrointestinal tract activity appears to be a function of the blood sugar level rather than the overall metabolic effect of diabetes. This seems confirmed by the findings that glucagon will induce elevations of blood sugar and a reduction in gastric activity. Melrose found that glucagon will inhibit spontaneous secretion of gastric acids, and yet will not inhibit the acid output obtained in a "maximum" histamine response.¹⁶ This suggests that the effect of the glucagon hyperglycemia is not peripheral, at the level of the gastric mucosa, but is central. Mayer has reported that the central effect of hyperglycemia is on the gluco-receptor area. He found that glucagon hyperglycemia does inhibit the gastric contractions of normal rats, but does not inhibit the gastrointestinal motility of rats which have received damage to their ventromedial nucleus.¹⁵ This study provides confirmation that elevation of blood sugar can have a direct effect on the activity of the gastrointestinal tract, and that this change in activity requires that the gluco-receptor area remain intact.

Integration of Observations

When we integrate the overlapping areas of study of these two groups, we find a useful proposition for the biologic basis of the protection which diabetic patients have against peptic ulcers. The hypothalamus must remain intact in order to continue its normal and integrated activity. The effect of destructive lesions will be to interfere with the balance of activity of the hypothalamus as a whole. When an inhibiting area is destroyed, the effect will appear as if stimulation had occurred, since the activity of the hypothalamus will continue without the negative feedback from the destroyed area. There can be similar paradoxical results when stimulation is applied to such an area. The effect of stimulation of an inhibitory area will be to diminish the hypothalamic activity. This has been found to be the case with respect to the activity of the ventromedial nucleus of the hypothalamus. Destruction of it causes increased activity of the feeding center, and the animal becomes hyperphagic. Stimulation of it will inhibit activity in the lateral hypo-



Fig. 2—This illustration of the hypothalamus indicates the location of the ventromedial and arcuate nuclei which are cross-hatched. The arrows indicate negative feed-back circuits which are activated by hyperglycemia, and inhibited by hypoglycemia.

thalamus.¹³ This nucleus has been found to be part of the gluco-receptor area; it can be stimulated by elevation of the blood sugar level, inhibited by hypoglycemia. It is proposed that the inhibitory effect which follows elevation of blood sugar is not limited to the lateral hypothalamic feeding area but also includes the adjacent anterior hypothalamic area which is involved with the development of peptic ulcers.⁹ Elevations of blood sugar have been found to inhibit gastrointestinal tract activity,¹⁵ and to protect animals from development of ulcers during the alarm reaction.⁶ The blood sugar level is one of several factors which affect the function of the gastrointestinal tract. This information provides us with a basic foundation for increasing our understanding of the biologic basis for the protection which diabetes provides against the development of peptic ulcers.

Summary

The gluco-receptor mechanism has been found to be associated with the centromedial and arcuate nuclei of the hypothalamus. Activation of this mechanism by elevations of the blood sugar has been demonstrated to inhibit the feeding center of the lateral hypothalamus. It is proposed that activation of the gluco-receptor mechanism to inhibit the function of an adjacent nucleus is not limited to just the lateral hypothalamus. This inhibition will include the anterior and posterior hypothalamic areas as well.

mic areas as well.

Activation of the anterior hypothalamus is associated with the experimental production of peptic ulcers. If we accept the proposition of this paper, we must conclude that the activation of the gluco-receptor mechanism by hyperglycemia will cause an inhibition of the anterior area and protect against peptic ulcers. It has been clinically observed that diabetes protects against peptic ulcers, and that dextrose protects experimental animals against ulcers. These findings tend to support the proposition.

The findings relative to hypoglycemia provide us with further confirmation. Chronic hypoglycemia has been found to be a factor in the experimental production of ulcers, and the flat glucose tolerance curve which results in hypoglycemia has been repeatedly found in patients with peptic ulcers. The effect of hypoglycemia will be to diminish the activity of the ventromedial nucleus. When the activity of this negative feed-back inhibitory circuit has been diminished, adjacent areas will be released, and will tend to behave as they do when stimulated.

The blockade of an inhibitory circuit releases the "target area" to perform its inherent physiologic activity. When the anterior hypothalamus is activated, this parasympathetic center will act by the initiation of the cephalic phase of digestion if the vagus nerve is intact. The animal will then be prone to the development of peptic ulcers.

References

1. Wilder, Russel M.: Diabetes and Hyperinsulinism. W. B. Saunders Co., Philadelphia and London, 1940.
2. Berry, M.: Studies of the Unknown Factors in Duodenal Ulcer, Hypoglycemia as a Possible Etiologic Agent. Amer J Gastroent 27:31, 1957.
3. Abrahamson, E. M.: Hyperinsulinism as a Factor in Peptic Ulcer. Amer J Dig Dis 12:379, 1945.
4. Poth, E. J., and From, S. M.: The Relation of Pancreatic Secretions to Peptic Ulcer Formation, III. The Influence of Hyperglycemic Glycogenolytic Factor. Gastroenterology 16:490, 1950.
5. Selye, H., et al.: Recent Advances in the Experimental Productions of Peptic Ulcers. Canad Med Ass J 34:399, 1936.
6. Selye, H., and Maclean, A.: Prevention of Gastric Ulcer Formation During the Alarm Reaction. Amer J Dig Dis 11:319, 1944.
7. Foltz, E.: Neurophysiologic Mechanisms in Production of Peptic Ulcers. JAMA 187:413, 1964.
8. Porter, R. W., et al.: Hypothalamic Influences on Hydrochloric Acid Secretion of the Stomach. Surgery 33:875, 1953.
9. Pearl, J. M., et al.: Hypothalamic Stimulation and Feline Gastric Mucosal Cellular Populations, Factors in the Etiology of the Stress Ulcer. JAMA 195:281, 1966.
10. French, J. D., et al.: Gastrointestinal Hemorrhage and Ulceration Associated with Intracranial Lesions. Surgery 32:395, 1952.
11. Long, D. M., et al.: Hypothalamic Influences on Gastric Ulceration. Arch Neurol 7:167, 1962.
12. Anand, B. K.: Nervous Regulation of Food Intake. Physiol Rev 41:677, 1961.
13. Anand, B.; Dua, S.; and Singh, B.: Electric Activity of the Hypothalamic "Feeding Centers" Under the Influence of Changes in Blood Chemistry. EEG and Clin Neurophysiol 13:54, 1961.
- 14-16. May be secured from the author or the reprints.

If, in a woman pregnant with twins, either of her breasts loses its fullness, she will part with one of her children; and if it be the right breast which becomes slender, it will be the male child, or if the left, the female.—Hippocrates

YOUR HEALTH! MR. PRESIDENT

William McKinley (1843-1901)

Hostages to fortune, Bacon called us all; but our Presidents suffer double exposure to the proverbial "slings and arrows." In the case of four of our Presidents the agent of "outrageous fortune" was a bullet.

William McKinley was our twenty-fourth President, the fifth to succumb in office and the third of four to die by assassination. As a lad he was just a normal, healthy American boy: one single component of that anonymous reservoir from which our national public figures are destined to emerge. Sportswise he was proficient at marbles, adept at bow-and-arrow marksmanship, and avidly addicted to swimming.

Later at college, young seventeen-year-old William suffered a general physical collapse, from which indeterminate and non-specific malady he must duly have recovered, for at eighteen he joined the Ohio Volunteers to fight in the Civil War. Throughout his military service he appeared to have a charmed life: impervious to enemy fire and immune to camp fever. Further, as a bonus, he was awarded official recognition for heroism on the battlefield.

In manhood McKinley was a strikingly handsome and healthy specimen, with no other disability than a "tobacco heart." Cigars were his one and only indulgence; but he was meticulously careful never to be photographed with them in evidence. Alcohol he never touched.

On September 6, 1901, while standing in a receiving line at the Pan American Exposition in Buffalo, New York, McKinley was fired upon at close range by one Leon Czolgosz as the two men were apparently about to shake hands. Two shots hit the President: one bullet flesh-grazing his chest and later dropping from his clothing; the other bullet entering his body above the navel. Surgical exploration through a five-inch incision showed that the bullet had passed through the stomach, leaving a small smooth aperture where it entered and a large rough one where it exited—to lodge irretrievably somewhere in the back. Both stomach holes were carefully sutured, special care being taken that no stomach contents escape into the abdomen to cause peritonitis, the one complication the doctors dreaded most. The critical surgery lasted one hour and was performed with the only instruments at hand, those from a pocket case, the grim scene illuminated by the waning daylight intensified by and reflected from hand mirrors. The bullet was not recovered.

Late that night an official bulletin announced to the shocked and shaken nation: "The President is rallying satisfactorily and is resting comfortably. Temperature, 100.4; pulse, 124; respiration, 24." Early the following day the anxious country heard the optimistic report: "The President continues to rest well. Temperature, 101.6; pulse, 110; respiration, 24"; and on Monday, September 9 the reassuring: "The President's condition steadily improves and he is comfortable, without pain or unfavorable symptoms. Bowel and kidney functions normally performed."

By Wednesday McKinley had so markedly improved that he could eat. He even requested a cigar, which naturally was denied him.

But on Thursday the tide turned. Optimism yielded to pessimism as the President's condition began to deteriorate rapidly, a bulletin on Friday announcing: "The President is suffering from extreme prostration. Oxygen is being given. He responds to stimulation but poorly. Pulse, 125; respiration, 40." The end came early the following morning.

A touching note is poignantly recalled by the writer of this monograph: McKinley's request as the final shadows deepened, that the window shade in his room be

Continued

raised to admit more light. Incidentally, his favorite hymn was Lead, Kindly Light.

The autopsy report, signed by two U. S. Army surgeons and eleven other attending doctors, stated:

"The bullet which struck over the sternum did not pass through the skin and did little harm. The other bullet passed through both walls of the stomach near the lower border. Both holes were found closed by the stitches, but the tissue around each hole was gangrenous. After passing through the stomach, the bullet passed into the back walls of the abdomen, hitting and tearing the upper end of the left kidney. This portion of the bullet track was also gangrenous, the gangrene involving the pancreas. The bullet was not found. There was no sign of peritonitis or disease of other organs. The heart walls were very thin. There was no evidence of any attempt at repair on the part of nature, and death resulted from the gangrene which affected the stomach around the bullet wounds as well as the tissue around the further course of the bullet."

With acknowledgments to Karl C. Wold, M.D.: Mr. President—How Is Your Health? 1948.

What's New!

Parke, Davis & Company announced recently that it had added three new sizes of Redi-Wrap Gauze Sponges, Sterile to its expanding line of medical-surgical products.

The new sizes of gauze sponges are put in Sponge-Control Envelopes, each containing two sponges.

Each package of Redi-Wrap Gauze Sponges is code-colored red, is tamperproof to assure sterility, and features ready-to-use convenience.

UNIMATIC packaging of tablets and capsules is now available from E. R. Squibb & Sons, Inc.

The importance of drug distribution systems in the UNIMATIC package is a means of providing a more efficient, better control over drugs. The new UNIMATIC tablet and capsule form will be supplied in strips of ten, with ten strips per compact box.

Squibb also markets a unit-dose disposable syringe under the UNIMATIC trade name.

TALWIN (pentazocine), a non-narcotic analgesic, has been approved by the FDA. This drug has been effective in doses of 30 milligrams given by injection, approximating the effectiveness of ten milligrams of morphine. Testing in the United States over the past nine years has indicated the drug to be well tolerated with a low incidence of side effects. Mild sedation has accompanied the pain relief in many instances. Tolerance and addiction are not reported and because the new preparation is not a narcotic, it has the additional advantage of being dispensable without inventory control. (Winthrop Laboratories)



Editorials

Fractures of the Mandible*

THIS DIAGNOSIS and treatment of mandibular fractures may appear, at first, to be simple and uncomplicated. The cardinal objective in treatment is the restoration of function performed by the dental and supporting structures of the dental complex. The technical procedures by which this objective may be accomplished are numerous. Two fundamental factors, however, are necessary for successful treatment: proper reduction and adequate immobilization.

No one method of treatment will give proper reduction and adequate immobilization in every patient. The age and health of the patient may perceptibly influence the treatment plan; correspondingly, the ability and experience of the surgeon may bias the selection of a certain technical procedure. Finally, the circumstances under which the patient is treated may render selection of one method over that of another more advisable.

Historically, the cliché, "The simplest is the best," has been considered to be synonymous with competent treatment of mandibular fractures. Although this cannot be challenged in principle, in reality the simplest treatment may be undertreatment; and undertreatment is often appended by postoperative problems. For example, closed reduction of mandibular symphyseal fractures is simple, but unfortunately this method often allows the segments at the inferior border of the mandible to spread. At best, malunion may occur, and the possibility of nonunion

is recognized. Adequate immobilization of these fractures may often be accomplished by means of a trans-osseous wire placed below the apices of the teeth. This may be performed intra-orally, thus eliminating the necessity of an extra-oral incision.

Extra-oral skeletal pinning is not as obsolete as some authors have indicated. There are selected fractures in which this procedure is an excellent modality of treatment, and the knowledge and ability to utilize this technique should perhaps be mastered by anyone who treats facial trauma. The older appliances were definitely

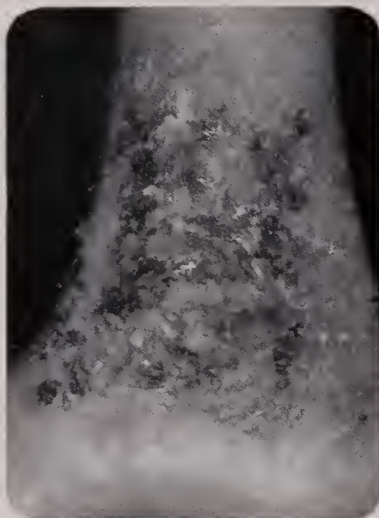


Use of quick-curing acrylic for stabilization of pins.

Continued

*Fitz-Hugh, G. S.: Fractures of the Mandible. Minnesota Med 50:981, 1967.

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Administration and Dosage: Apply sparingly to the affected area 3 or 4 times daily. Some cases of psoriasis may be more effectively treated if the 0.1% Cream or Ointment is applied under an occlusive dressing.

Contraindications: Tuberculosis of the skin, herpes simplex, chicken pox and vaccinia.

Precautions and Side Effects: Do not use in the eyes or in the ear (if drum is perforated). A few individuals react unfavorably under certain conditions. If side

effects are encountered, the drug should be discontinued and appropriate measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive non-permeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyodermas will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

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cumbersome to the patient and too expensive for the surgeon to place indiscriminately. However, the biphasic pinning technique incorporates quick-curing acrylic plastic for stabilization of the pins (Figure); this makes possible lighter appliances, more comfort for the patient, and less investment in equipment. In addition, this technique allows the continued use of the mandible, thus eliminating the need for intermaxillary fixation.

Decisions regarding teeth that are in the line of a mandibular fracture are often difficult. If the fracture occurs at the angle of the mandible and transverses an impacted third molar, it is frequently advisable to remove the impacted tooth and, at the same time, set an intra-osseous wire (intra-orally) in place. There are certainly some indications for retaining an impacted tooth, for example, when the tooth prevents displacement of the proximal segment. In this situation the patient should be given antibiotic coverage until good healing has been observed. This period of antibiotic coverage may well correspond to the period of immobilization.

Recommendations regarding length of immobilization of the fractured mandible vary among traumatologists. Although six weeks is an average length of immobilization, it is not the maximal period that can be tolerated physiologically. Certainly the type of fracture, associated medical problems, and the age of the patient all serve as guidelines for decisions regarding length of

immobilization. Often it may be advantageous to leave the arch bar or mandibular splint attached to the teeth for a week (or longer) immediately after removal of intermaxillary fixation. This allows for observation during the initial period of returning function of the mandible.

My final thoughts concern mandibular fractures of children. Fortunately, such fractures are infrequent. As is true for older patients, individual circumstances dictate the most advisable treatment plan. It has been found efficacious, however, to utilize an appropriate stock bite index. The unique occlusion of the patient is determined and maintained by means of an impression compound or a quick-curing acrylic. The mandibular occlusal index is then stabilized with circummandibular wires. This procedure, when indicated, has obvious advantages and is well tolerated by pediatric patients.

In the final analysis, there is a myriad of variations of technical procedures for treatment of mandibular fractures. The successful treatment encompasses those techniques that will ultimately restore occlusion and function of the masticatory apparatus. The key to successful treatment revolves around the surgeon's knowledge of the occlusion of his patient, whether the dentition is deciduous, mixed, or permanent.

Bruce A. Lund, D.D.S.
Rochester, Minnesota

Gastrocamera

DR. BARTNESS* reports on the radiological accuracy of distinguishing benign and malignant gastric ulcers. He reported 98 per cent accuracy, in a series of 150 gastric ulcers, in differentiating benign from malignant ulcers solely by radiological techniques. This result is at variance with that reported by others.^{2,3,5} The discrepancy may be explained on the basis of the more advanced radiological equipment and techniques used by Bartness. However, only four of the ulcers were malignant in his series. If all the ulcers were diagnosed as benign the accuracy would still be 97 per cent. Of the seven gastric ulcers that were diagnosed as malignant radiologically, only four were proven to be histologically malignant.

In the last few years there has been a resur-

gence of interest in gastroscopy and intragastric photography. Although high quality photographs had been made through the standard gastroscopy, the procedure was cumbersome and not readily applicable to routine use. The first practical gastrocamera was developed in Japan in 1950 by Drs. Uji and Hayashida of the University of Tokyo and the Olympus Optical Company of Tokyo. The first extensive clinical evaluation began in the United States in 1962 by Morrissey and co-workers¹ at the University of Wisconsin. They used the Olympus Gastrocamera Model GT V which was lowered into the stomach, and blind photographs were taken from several different positions. The camera is located in the distal end of the tube which has a removable tip for insertion of the film cassette. Thirty-two individual colored pictures can be obtained from a

Continued

*Bartness, John: Benign and Malignant Gastric Ulcers. Minnesota Med 50:505, 1967.



*"When I couldn't even smell corned beef and cabbage,
I decided it was time for you, Doc."*

Maybe he doesn't know when he's well off. But you might want to prescribe long-acting Novahistine LP anyway.

Two tablets in the morning and two in the evening will usually provide day and night relief by helping to clear congested air passages for normal, free breathing. Novahistine LP is formulated to provide continuous therapeutic effect for 8 to 12 hours. The decongestant ingredients help restore normal mucus secretion and ciliary activity—physiologic defenses against infection of the respiratory tract.

Use cautiously in individuals with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Caution ambulatory patients that drowsiness may result. Each Novahistine LP tablet contains: phenylephrine hydrochloride, 25 mg., and chlorpheniramine maleate, 4 mg.

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5 mm. film cassette. A small flash lamp is housed in the camera beyond the lens and can be activated by the examiner. There is a flexible joint above the camera which permits the camera unit to be tilted up or down 35 degrees from a horizontal plane. The latest version is the Olympus Model GTF which contains an image-carrying bundle of fiberglass and an objective lens which covers approximately the same field as the gastrocamera lens. This instrument therefore allows gastroscopic examination and intragastric photography simultaneously.

In contrast to conventional gastroscopy, the procedure is not difficult and produces a minimum of patient discomfort, as the gastrocamera tube is soft and flexible. It can also be used repeatedly in the same patient.

In a series of 62 benign gastric ulcers, Morrissey et al.,² using the Olympus GT V gastrocamera, gastroscopy and X ray, found 66 per cent diagnosed by X ray, 58 per cent by gastroscopy, and 74 per cent by gastrocamera. The addition of the gastrocamera to X-ray studies increased the accuracy to 95 per cent. Hara et al.,³ in a study of 1100 patients with some gastroenterological complaints, found gastric ulcers in 204 and gastric cancer in 107. In the ulcer group, the X ray and gastrocamera were each positive in 60.5 per cent; 12.8 per cent were negative by X-ray examination but found by the gastrocamera. Most of

the latter group were small, shallow ulcers. In the group of 107 gastric carcinomas, positive results by both X ray and gastrocamera were found in 86 per cent. The gastrocamera failed in 6.5 per cent while the failure rate was 7.4 per cent by X ray. Chrysospathis⁴ reported the correct diagnosis in 121 of 126 benign gastric ulcers and 66 of 71 gastric carcinomas using the gastrocamera. From Australia, Milton, Lynch and Skyring⁵ reported 250 cases of gastric pathology and obtained a high percentage of accuracy with the gastrocamera, especially in diseases of the antrum and the lesser curvature. The gastrocamera has also been useful in the diagnosis of gastritis and gastric atrophy and in the detection of other forms of gastric pathology such as benign and malignant polyps, leiomyomas and phytobezoars.*

Although there is much to support the value of the Olympus Gastrocamera GT V as a blind procedure, the development of the Olympus GTF Gastrocamera, which permits gastroscopic examination and simultaneous intragastric photography, provides additional accuracy in the diagnosis of gastric lesions.

Gastroscopy and gastrocamera studies are not intended to replace radiological examination; indeed they are ideally complementary and will provide a higher degree of diagnostic accuracy of gastric pathology.

Elliot M. Latts, M.D.
Minneapolis, Minnesota

*See Test Your Word Score Page 1359.

References

1. Perna, G., Honda, T., and Morrissey, J. F.: Gastrocamera Photography. *Arch Intern Med* 116:434, 1965.
2. Morrissey, J. F., Honda, T., Hara, Y., Juhl, J. H., and Perna, G.: The Use of the Gastrocamera for the Diagnosis of Gastric Ulcer. *Gastroenterology* 48:711, 1965.
3. Harra, Y., Ogoshi, K., Karasawa, K., Osawa, G., Yokoyama, Y., and Ansfield, F. J.: Clinical Experience with the Gastrocamera. *Amer Surg* 159: 542, 1964.
4. Chrysospathis, P.: Gastric Camera. *Surgery* 54:292, 1963.
5. Milton, G. W., Lynch, A., and Skyring, A. P.: The Diagnosis of Gastric Lesions. *Brit J Surg* 52:607, 1965.

Oral Contraceptives

STEROIDS ARE currently being taken orally for contraceptive purposes by six or more million women in the United States. Repeated studies with each of the compounds leave no doubt about their contraceptive efficacy.

Considering that the prototypes of the two active ingredients in the oral contraceptive medications are estrogen and progesterone and that

the production of these two hormones increases during pregnancy, one might expect the medications to produce the physical symptoms and the changes in organ function which one would normally associate with pregnancy.

Initial concern about the safety of these agents was directed to their effects on blood coagulability. It is generally agreed that with the use of these

Continued



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Mike expects a penicillin injection. He's about to be pleasantly surprised.

His physician is going to prescribe an oral penicillin —PEN·VEE® K (potassium phenoxymethyl penicillin). It's usually so rapidly and completely absorbed that therapeutic serum levels are produced in 15 to 30 minutes. Higher serum levels generally last longer than with oral penicillin G.

Indications: Infections susceptible to oral penicillin G; prophylaxis and treatment of streptococcal infections; treatment of pneumococcal, gonococcal, and susceptible staphylococcal infections; prophylaxis of rheumatic fever in patients with a previous history of the disease.

Contraindications: Infections caused by nonsusceptible organisms; history of penicillin sensitivity.

Warnings: Acute anaphylaxis (may prove fatal unless promptly controlled) is rare but more frequent in patients with previous penicillin sensitivity, bronchial asthma or other allergies. Resuscitative (epinephrine, aminophylline, pressor amines) and supportive (antihistamines, methylprednisolone sodium succinate) drugs should be readily available. Other rare hypersensitivity reactions include nephropathy, hemolytic anemia, leucopenia and thrombocytopenia. In suspected hypersensitivity, evaluation of renal and hematopoietic systems is recommended.

Precautions: In suspected staphylococcal infections, perform proper laboratory studies including sensitivity tests. If overgrowth of nonsusceptible organisms occurs (constant observation is essential), discontinue penicillin and take appropriate measures. Whenever allergic reactions occur, withdraw penicillin unless condition being treated is considered life threatening and amenable only to penicillin. Penicillin may delay or prevent appearance of primary syphilitic lesions. Gonorrhea patients suspected of concurrent syphilis should be tested serologically for at least 3 months. When lesions of primary syphilis are suspected, dark-field examination should precede use of penicillin. Treat beta-hemolytic streptococcal infections with full therapeutic dosage for at least 10 days to prevent rheumatic fever or glomerulonephritis. In staphylococcal infections, perform surgery as indicated.

Adverse Reactions (Penicillin has significant index of sensitization): Skin rashes, ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; serum sickness-like reactions, including chills, fever, edema, arthralgia and prostration. Severe and often fatal anaphylaxis has been reported (see "Warnings").

Composition: Tablets—125 mg. (200,000 units), 250 mg. (400,000 units), 500 mg. (800,000 units); Liquid—125 mg. (200,000 units) and 250 mg. (400,000 units) per 5 cc.

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medications there is an increase in factor VII level. Increases in levels of factors VIII and X and fibrinogen have been reported to occur sporadically. Studies of hepatic function have shown inconsistent increases in serum bilirubin, alkaline phosphatase, glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase, and impaired excretory capacity for sulfobromophthalein. Thyroid function studies have shown increased levels of protein-bound iodine, butanol-extractable iodine, and thyroxine-binding globulin, and a decrease in erythrocyte triiodothyronine-binding coefficient. There has also been reported increased secretion of aldosterone and increased plasma cortisol levels.

Dr. Spellacy* has previously demonstrated that women taking large doses of norethynodrel with mestranol (Enovid) have increased fasting blood sugar and plasma insulin levels. Now he and his

*Spellacy, W. N., Birk, S. A., Noer, K. A., and Schade, S. L.: Sedimentation Rate in the Normal Menstrual Cycle or with Oral Contraceptive. *Minnesota Med* 50:645, 1967.

co-workers have shown that these medications can cause an increase in the average erythrocyte sedimentation rate, although the range of values remains essentially the same as in nonusers.

The significance of the problem potentially inherent in the use of oral contraceptives seems to lie in (1) whether or not persistence of these changes for long periods is harmful and (2) whether or not these changes would persist after cessation of use of the compounds.

The above changes are reported to occur less constantly and to a lesser degree than in pregnancy. Because there is currently no evidence that these changes are harmful or persist after cessation of use of the compounds, after short or prolonged use, the major consideration at the present seems to be an awareness of the effect of these drugs on the various laboratory studies and a cautious interpretation of the results when the patient being studied is taking oral contraceptive medication.

George D. Malkasian, Jr., M.D.
Rochester, Minnesota

Non-Symptoms

A SYMPTOM can be defined for medical purposes as the subjective evidence of illness.* It is a useful word denoting that portion of disease which disturbs the patient. Throughout history physicians have studied the symptoms of disease and given utmost consideration to their description by the patient. Their presence often dictates the treatment, and absence of symptoms may be the decisive influence against therapy. In the field of symptomatology there is another useful concept not well defined in medicine which can be labeled the non-symptoms. These are the evidences of disease which usually are the cause of the patient's complaint but for various reasons are ignored, suppressed, or otherwise not recognized. Meador's discussion on non-disease¹ stimulated this essay on non-symptoms. Although non-disease implies no disease, non-symptoms, on the other hand, cannot be equated with no disease.

A 67-year-old man complained of recurrent episodes of syncope. He denied dyspnea or an-

gina. No disturbance in mood was detectable. The pulse rate was 28-30 per minute. An electrocardiogram showed an atrial rate of 60 with a variable 2:1 and complete A-V block with ventricular rate as above. A transvenous pacemaker was implanted in the right infraclavicular space, threaded into the right ventricle, and set to drive the heart at 70 beats per minute. The next day the pulse was 70 and regular, and a remarkable improvement was evident. The patient was euphoric, stating he was no longer depressed. Shortness of breath and a feeling of constant pressure in the chest were gone. When asked why he had not previously mentioned his mental depression, chest pain, and angina, he stated that he was much more aware of these symptoms after their sudden subsidence. However, he now had a new and original complaint. The site of the batteries would interfere with the seating of his rifle and might spoil deer hunting in the fall. This non-symptom is of social rather than medical importance.

Non-symptoms pervade every field of medicine. The child with a congenital disorder recognizes his symptoms only upon relief. The victim of

Continued

*The definition of symptom in Merriam-Webster 2nd Edition and in Dorland's 24th Edition does not differentiate between symptom and sign. Current medical usage, however, favors the use of sign for an objective finding and symptom for a subjective complaint.



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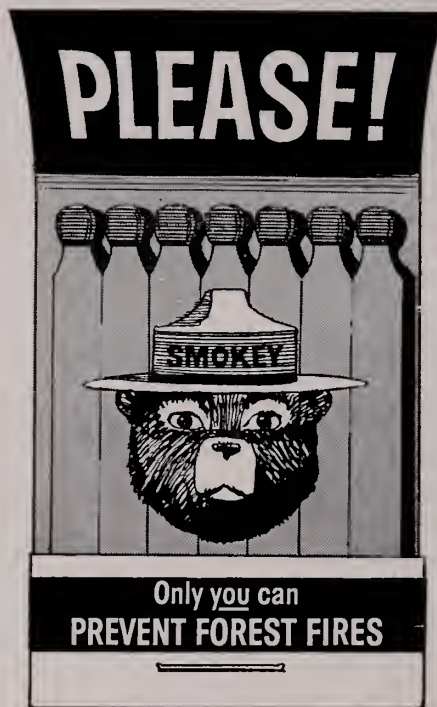
Pectin (2½ grains) 162 mg.

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insidious disease may complain very little, not recognizing imperceptible changes. Thus a patient with mitral disease may describe weakness and inability to climb stairs only after the valve has been corrected. The non-symptoms are then recognized as real symptoms.

Dissimulation leads to another form of non-symptom. An example is the absence of angina pectoris among licensed pilots. These men may have myocardial infarction, but angina of effort in flying personnel is a curiosity. Perhaps the loss of the license to fly, attendant upon the disclosure of the symptom, is a factor in producing a non-symptom.

Fear can suppress symptoms. Many patients visit their physician to be reassured that they are free of disease. Like a school boy mouthing an

answer to please the teacher and get a good grade, the patient may give the "right" answers that give him the "A" in health he fervently seeks. A 60-year-old man came to the doctor's office for a routine physical examination. He denied all symptoms. He submitted to an examination but refused a rectal examination. The persistent physician finally obtained consent for this procedure. As the patient dropped his shorts he volunteered the information: "You know, doctor, I've had a little bleeding down there the last few months." Fortunately his rectal cancer was resectable. The physician alert to the non-symptoms realizes there is no routine physical examination. There is only the failure to discover the complaint.

Reuben Berman, M.D.
Minneapolis, Minnesota

Reference

1. Meador, C. K.: The Art and Science of Non-disease. *New Engl J Med* 272:92, 1965.

Test Your Word Score

Enteropathogenic—*originating in the intestine* (page 1312).

Conceptual—*pertaining to an opinion* (page 1315).

Hydrogenated—*hydrogen added to* (page 1323).

Papyraceous—*like parchment paper* (page 1325).

Stercoral—*fecal* (page 1331).

Diapedesis—*outward passage through intact vessel walls of corpuscular elements of the blood* (page 1333).

Telangiectasia—*dilatation of terminal vessels* (page 1336).

Phytobezoar—*a gastric concretion composed of vegetable or fruit seeds, skins, etc.* (page 1355).

Euthyroid—*normally functioning thyroid* (page 1402).

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You May Be Right

In an editorial, entitled "An Obstetrician Proposes a Change in the Abortion Laws," MINNESOTA MEDICINE, May 1967*, the writer states that "therapeutic abortion is not needed as a solution to the problem of pregnancies resulting from rape" and says further that "we as physicians are now able to effectively prevent pregnancies up to 48 hours after intercourse by the use of an estrogenic substance." He draws this conclusion from a paper by Morris published in the American Journal of Obstetrics and Gynecology, 96:804, 1966.

I would like to take issue with this point of view on two grounds. A careful reading of the original paper by Morris leaves much doubt as to the efficacy of this type of "medical abortion" and, secondly, evidence from a Professor of Law at the University of Minnesota indicates that if physicians in this state use such means to prevent pregnancies resulting from rape, they may be risking up to four years of imprisonment, if convicted, under the present statute dealing with abortion in Minnesota.

In the original paper by Morris, he states that certain rape cases were given 50 mg. of stilbesterol for four to six days after exposure and that "in this *small* series of cases no patient has become pregnant so far." He further says that the side effects of this dosage of oral estrogen were undesirable because of nausea and mastodynia. He comments: "In these *preliminary* trials there have been no pregnancies. These clinical studies are *incomplete* and have as yet *no* statistical significance." He then continues: "These agents *may* inhibit implantation of the fertilized ovum. Because there may be undesirable side effects of estrogens in high doses, practical clinical use at present would be *limited*." His conclusion is that "these results should be viewed with caution."

It seems clear then that the administration of high-dosage estrogen preparations within 48 hours of exposure is still in the experimental stage and that Morris' work should not be interpreted as conclusive evidence that these preparations will prevent pregnancy in all instances. It should be remembered that there is no way of knowing whether women raped at midcycle would have become pregnant, since the chance of pregnancy following rape is uncertain for many obvious reasons. There can be no controls. Women, in order to take advantage of this method of preventing these unfortunate pregnancies even if it were to prove uniformly reliable in all instances, would have to be treated by physicians within 48 hours after intercourse.

There are those who demand legal "proof" of criminal assault before they will accept the "alleged" rape and interfere with the pregnancy. How could this proof be obtained within 48 hours of exposure? The legal process is by necessity slow; adjudication within 48 hours is impossible. Many women are reluctant to report cases of rape the moment it takes place, because of the social stigma involved and the failure to prosecute in most cases of rape. I would therefore suggest that even if high-dose estrogen administration could always prevent implantation of the fertilized ovum, the use of this modality would be limited.

There are also serious legal questions involved in administering such medication under Minnesota's present abortion statute, which makes it a felony to "administer to a female, whether pregnant or not, any medicine, drug or substance with intent thereby to produce miscarriage."

Professor Maynard Pirsig, Professor of Law, University of Minnesota, has

*See Page 689.

Continued

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written that "Chitty's Medical Jurisprudence states that the expulsion of the ovum or embryo within the first six weeks after conception is technically called miscarriage. If the use of the term miscarriage is proper, then the meaning of the present statute makes the practice of administering a hormone an abortion. I have found no authorities to the contrary that would lead to a different conclusion."

I would therefore urge the physicians of this state to carefully read Professor Morris' paper and Professor Pirsig's opinion before resorting to the use of high-dosage estrogen to women who have been raped. Let me also respectfully remind those physicians who believe that life begins at the moment of conception that, in order to be consistent, they cannot advocate the use of any drug or substance which will prevent implantation of a fertilized ovum. The moral issue remains whether this is to be done medically or surgically.

In the light of Professor Pirsig's opinion, when doctors of the highest reputation of this state are put in this predicament, acting in accordance with their highest ethical principles, it would seem vitally important that the present abortion statute be changed and changed promptly.

Fred A. Lyon, M.D.
Minneapolis, Minnesota

The Editor's Soliloquy

Two Blaud's -- Bed Socks -- Stat!

My hypothetical patient in the hospital with acute hemorrhagic anemia doesn't want all those needles in her arms and legs and those bottles of blood overhead; she wants two Blaud's, Stat! And for that postoperative pulmonary congestion and hyperpyrexia: no tubes down her throat to make her cough her head off; she's catching cold and wants bed socks!

When told to trim down and take off weight: that's O.K. if she doesn't have to cut down on calories. Who wants to deprive oneself? Why can't she have shots instead!

For her little aches and pains why can't she have those daily infra treatments—like the neighbor's wife has been 'enjoying for a year and a half now—exclusive of Saturdays, Sundays, and holidays. If they weren't helping her it stands to reason she'd stop having them, wouldn't she!

Carl O. Rice, M.D.

Old Doc Hess says: There are occasions when nothing serves quite so well as an appropriate 4 or 5-letter word!

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Curbstone Consultation

QUESTION: A 32-year-old woman patient of mine was recently in for a checkup. The examination was entirely negative and she was feeling well. However, a serum protein-bound iodine was reported to be 9.0 mcg.%, and repeated was 9.5 mcg.%. A thyroid I^{131} uptake was then done and reported as normal. A T_3 resin test was in the hypothyroid range. She has not received any iodine-containing drugs or x-ray contrast material, and her only medication is "Enovid" for contraception. She has had a small diffuse goiter since her first pregnancy ten years ago. Do you think she has any thyroid disease, and if so what can I do further to make a diagnosis?

ANSWER: First of all, pregnancy is associated with an elevation of plasma thyroid-binding globulin and as a result, an increase in serum protein-bound iodine and a decrease in T_3 resin uptake. The thyroid I^{131} uptake is normal. Small, diffuse, asymptomatic goiters commonly occur during pregnancy. These changes usually return to normal within six to eight weeks after delivery, although the goiter may persist. The administration of estrogens, including the contraceptive pills, produce these same changes except for the goiter.

The abnormalities found in your patient are most likely due to the contraceptive pill she is taking. Stopping the "pill" for four to six weeks and repeating the tests would establish this, although in a clinically euthyroid patient, I do not feel this is necessary. I would, however, make certain she is not pregnant.

Alvin L. Schultz, M.D.
Minneapolis, Minnesota

QUESTION: A 46-year-old man presented with a painless mass, about walnut size, at the base of his neck. He stated that it had arisen over night, and it was slightly tender. A ^{131}I scan revealed an area of hypoconcentration of radioactivity over the mass. Over a period of three weeks the mass became smaller without therapy. At that juncture, it was removed.

ANSWER: At surgery a hemorrhagic adenoma was discovered. The mass was a thin-walled cyst with an organizing hematoma in it.

The sudden appearance of a tender mass in the thyroid should always oblige one to consider the diagnosis of hemorrhagic adenoma.

Robert A. Maslansky, M.D.
Minneapolis, Minnesota

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The Viewing Box

Pyuria with Negative Urine Culture

The films below were made on a sixteen-year-old high school student. Figure 1 is the film made before the injection of the contrast media and Figure 2 is the twenty-minute excretory urogram. This lad was completely asymptomatic. Pyuria was noted on a urinalysis performed as part of a physical examination. A routine urine culture was reported as negative and a ten-day course of sulfisoxazole had no effect on the pyuria. At this point the films were made.

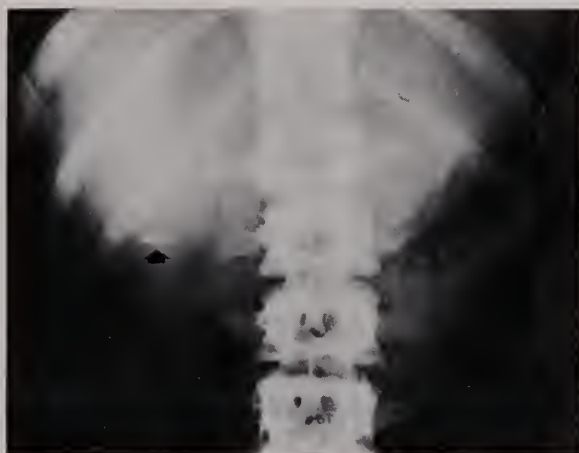


Figure 1



Figure 2

What is your diagnosis? (See next page.)

Diagnosis: Tuberculosis of the right kidney. Both smear and culture of the urine were positive for tubercle bacilli.

Renal tuberculosis is usually asymptomatic until the bladder or the epididymis becomes involved. With a negative routine urine culture and significant pyuria that does not respond to treatment, the diagnosis of tuberculosis should be entertained. The large ring-like calcification (arrow, Figure 1) overlying the right kidney represents a cold abscess. The non-function of the upper pole on the right is a result of tuberculous stricture (arrow, Figure 2) of the infundibulum to the upper pole calyx. Both of these x-ray findings are typical of renal tuberculosis.

Everette Duthoy, M.D.*
Minneapolis, Minnesota.

*Division of Urology, Hennepin County General Hospital.

Eleventh Annual Fellowship Program Announced by Wyeth Laboratories

Applications for two-year Wyeth Pediatric Fellowships are available now for residencies commencing July 1, 1968, it has been announced by the chairman of the Selection Committee, Philip S. Barba, M.D., past president of the American Academy of Pediatrics. All applications for this, the eleventh group of Fellowships, must be in the hands of the Committee by December 1, 1967.

Sponsored by the Wyeth Fund for Postgraduate Medical Education, each of these fellowships provides \$4,800 over two years toward the advanced training required for board certification in pediatrics. Wyeth's monthly payments, made directly to recipients, are in addition to the usual stipends paid to residents by the institutions in which they train.

Eligible to apply are interns, physicians who have recently completed an internship, research Fellows, or physicians completing their tour of duty with the Armed Services or the U.S. Public Health Service. Applicants must be citizens of the United States or Canada. Those who have already started Pediatric Residency training are not eligible. In the first nine years of this Fellowship program, 176 physicians have received its assistance toward their advanced training.

Each Fellow may choose the hospital in which he will train provided that it is accredited by the Residency Review Committee which represents the American Board of Pediatrics, the American Academy of Pediatrics, and the Council of Medical Education and Hospitals of the American Medical Association.

A voluntary committee of pediatricians, headed by Dr. Barba, Adjunct Professor of Pediatrics at Temple University School of Medicine and Emeritus Associate Professor of Pediatrics at University of Pennsylvania School of Medicine, has the responsibility of choosing the Pediatric Fellows. The committee considers the following factors: evidence of good character, academic achievement, performance of duties, and need for financial assistance. Wyeth plays no part in the selection of recipients.

Wyeth Laboratories inaugurated this Fellowship program in 1958 to encourage interns and other young physicians who want to specialize in pediatrics, who have proven abilities, but who would find it difficult to finance the required post-graduate training.

Heredity is nothing but stored environment.—Burbank



Tumor Conference

Eosinophilic Granuloma

EOSINOPHILIC GRANULOMA belongs to that group of diseases known as the proliferative reticuloendothelioses, histiocytoses, or reticuloses. In addition to involvement of the reticular tissue, there may be widespread systemic involvement including that of lung or bone. The following is the case history of a patient who, when first examined, showed involvement of both lung and bone without other evidence of the disease.

Case Report

A 17-year-old white boy was first seen in January 1966 because abnormalities were noted in a chest film. This chest roentgenogram had been made elsewhere one month previously because of a minor shoulder injury incurred during a school basketball game. The patient was asymptomatic. The only past history of importance was that he had spent several weeks as a "shaver" in a furnace during the previous summer.

The physical examination revealed a vigorous young male in no distress. There were no skin lesions or palpable nodes, and the liver and spleen were not palpably enlarged. The lungs were clear to percussion and auscultation.



Fig. 1—Posteroanterior view of the chest taken four years previously and reported as indicating normal findings.



Fig. 2—Posteroanterior view of the chest taken on admission to the clinic, showing fine, nodular opacities and diffuse, reticular pattern of infiltration.

Continued

The laboratory findings were within normal limits with a white blood cell count of 7500 and a normal differential count. The serum electrophoretic pattern was normal. Results of the PPD skin test, fungal skin tests, and the sputum cytology were negative.

The original film showed finely nodular opacities widely distributed throughout both lungs with a diffuse reticular pattern of infiltration. In addition, a well-defined lytic process involved the first thoracic vertebra. A chest film taken four years previously (Figure 1) was reported normal. A repeat chest roentgenogram (Figure 2) showed abnormalities similar to those described in the presenting film. A coned-down film of the cervicothoracic spine (Figure 3) confirmed the presence of a lesion involving the posterior elements of the first thoracic segment with an intact vertebral body. The skeletal survey revealed no other osseous involvement.

An open biopsy of the laminae and the spinous process of the first thoracic segment was performed. The diagnosis of the pathologist was eosinophilic granuloma, fibrosis and reaction, and new bone and cartilage formation.

Radiation therapy was instituted, and 1500 rads were delivered to the bony lesion. Subsequently, corticosteroid therapy was initiated because of the extensive pulmonary involvement. The patient was still asymptomatic six months later. A follow-up chest film (Figure 4) showed an apparent improvement in the bone lesion, while the pulmonary findings were unchanged.

Discussion

The pathological indications of eosinophilic granuloma of bone have been well described in several reports.^{1,2,6} The basic lesion is localized in the medullary cavity of the bone; as it expands it erodes and perforates the cortex and may then involve neighboring soft tissue. Thus the picture may be very similar to that of a malignant bone tumor.

Extraskelatal Disease

Although the term eosinophilic granuloma was originally applied to bone lesions with eosinophilic and histiocytic infiltration,⁶ extraskelatal manifestations have been recognized,⁸ and indeed it is now accepted that 20 per cent of all such bone lesions have associated pulmonary involvement.¹⁰ This has been demonstrated by lung biopsy or, as in our patient, by bone biopsy. The spectrum of pathological changes in the lung has been described in several reports.^{4,5}

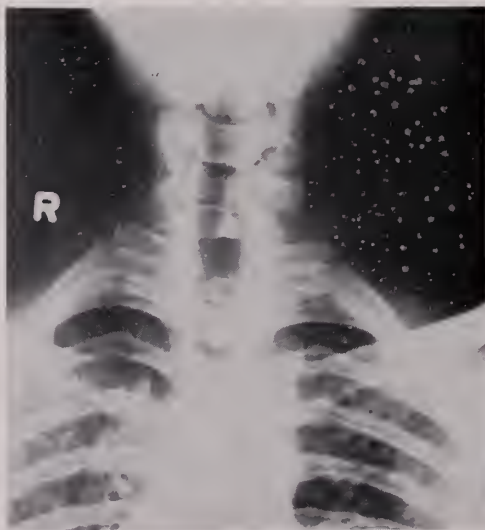


Fig. 3—Coned-down study of cervicothoracic spine showing lytic process involving first thoracic vertebra.



Fig. 4—Posteroanterior view taken at follow-up visit six months after first being seen. Findings are essentially unchanged from those on film taken at first admission.

The roentgenographic changes of eosinophilic granuloma in bone have been reviewed by Ochsner.⁸ The initial lesion is a localized area of rarefaction. The defect does not have a rim of sclerosis and represents the granuloma which has destroyed the bone. This looks very similar to the rarefaction due to other causes, and the distinction can only be made, as in our patient, by bone biopsy.

In the lung the roentgenographic changes show marked variability and may simulate many other diffuse infiltrative diseases.³ The picture may be one of generalized miliary infiltration, coarse nodulation, or reticulation. However, these changes can be limited to focal areas in the lung.⁵ Later changes include progressive fibrosis, perifocal emphysema, and "honey-combing."⁴ Subpleural bleb formation is believed to be responsible for the frequency of spontaneous pneumothorax as a complication of this disease.^{7,9}

Therapy and Prognosis

Most of the cases of eosinophilic granuloma are seen in childhood, adolescence, or early adult life. This condition usually causes some pain, though as a rule the pain is not severe.

Biopsy is generally required for a correct diagnosis.

According to Aegerter and Kirkpatrick,¹ this condition is usually regarded as an innocuous one, with the results of conservative treatment being good. It is important not to overtreat this type of benign tumor in the mistaken assumption that a malignant process is present.

Treatment is usually curettage with or without postoperative radiation therapy in moderate dosage.

Recently these patients have been treated with cortisone and various antimetabolic drugs with some degree of success.

However, the prognosis should be guarded if osseous as well as extraosseous lesions are present.

Summary

Eosinophilic granuloma may involve many systems, with simultaneous involvement of lung and bone. Our patient was entirely asymptomatic; diagnosis was established by bone biopsy. Therapy included radiation and corticosteroids.

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*Department of Diagnostic Radiology, Lahey Clinic Foundation.

References

1. Aegerter, E., and Kirkpatrick, J. A., Jr.: Orthopedic Diseases. Physiology, Pathology, Radiology. Second edition. Philadelphia, W. B. Saunders Co., p. 194, 1963.
 2. Auld, D.: Pathology of Eosinophilic Granuloma of the Lung. Arch Path 63:113, 1957.
 3. Gaensler, E. A.: Diagnostic Techniques in Diffuse or Miliary Lung Diseases; Experience with 381 Patients. In Banyai, A. L., and Gordon, B. L. (Editors): Advances in Cardiopulmonary Disease. Vol. III, Chicago, Year Book Medical Publishers, pp. 81-122, 1966.
- 4-10. May be secured from the authors or the reprints.

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Most medical fads are like some women's fashions—frail, fickle and costly.

—Noah Fabricant

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Neurological Conference

Idiopathic Epilepsy^{*}

Case Report

Doctor Todd Davis:**

This 18-year-old-boy was first seen at the University Medical Center in March, 1966, with the chief complaint of having had a convulsion three weeks previously. His first seizure occurred in June, 1962, and was accompanied by amnesia for events immediately preceding the attack. His brother told him that he had lain stiffly and then begun to shake all over. Following the seizure the patient was dizzy and lethargic. He had bitten his tongue but had not been incontinent. No apparent cause for his seizure was found at that time; nevertheless, his family physician placed him on $\frac{1}{2}$ grain phenobarbital three times daily as a precautionary measure.

In September, 1962, when he was evaluated at another clinic, no seizures had occurred since the initial attack. Although both the neurological examination and skull x-rays were normal, an electroencephalogram showed a generalized dysrhythmia in the temporal areas bilaterally. Since no obvious cause for his seizure had been found, it was elected to maintain him on the same phenobarbital dose.

Between September, 1962, and February, 1966, there apparently had been frequent intervals during which the patient neglected his medication. Although he was unable to relate a detailed history of his seizures, he undoubtedly has had several generalized seizures. Approximately three weeks before his visit to our Center in February, 1966, he had had another grand mal convulsion. At that time he had not taken his medication for one week preceding the seizure. In addition, he had been up quite late the night immediately prior to the attack and had only a little sleep the previous night. On the morning of that seizure he had had three lapses of consciousness lasting for five seconds each, then the generalized seizure occurred. When he awoke he found that his tongue was sore and he felt very tired; so he immediately went to bed. Finally his mother insisted that he go to the doctor.

Family History

Although the patient does not know any details of his birth history, he has had no other significant head trauma. In regard to childhood diseases, he has had both measles and mumps without complication and there has been no history of meningitis. It is interesting that three of his six siblings also have had seizures. At least two of the siblings had minor seizures which eventually progressed to major type seizures. A third sibling has had only grand-mal seizures.

Neurological Examination

Neurological examination of the patient in February, 1966, was completely within normal limits. His skull films showed no abnormality, but some slowing and depression of activity was evident in the right temporal area on the electroencephalogram. Again it was decided

^{*}Neurological Conference held February 23, 1967. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals.

^{**}Student Doctor, University of Minnesota Hospitals.

Continued

to continue him on the same phenobarbital dosage.

Progress

Four or five weeks later the patient came to the clinic stating that he had had two transient lapses of consciousness a few days earlier. He noted that he had been up late the preceding night and had forgotten to take his phenobarbital. Subsequently, in May, 1966, he stated that he was taking about two pills a day rather than three and also readily admitted that he frequently forgot to take his medication. Since he was complaining of symptoms of tiredness, his medication was changed from phenobarbital to a combination of dilantin and mebaral.

Another generalized convulsion occurred prior to his visit to our medical center in late October, 1966. Preceding this seizure he had forgotten to take his medication for a three-day period; however, as long as he took his dilantin and mebaral regularly, he had been seizure free.

During his most recent visit in late January, 1967, the patient stated that he had been taking his medications regularly and had had no seizures. He had brought a medical form which he wanted us to certify in order for him to obtain a driver's license. Also he was to be graduating from a vocational high school which he had been attending in Minneapolis and had already obtained a job with an electronics firm in the Twin Cities. Interestingly, there were only two students out of an original 35 that finished the electronics course from this vocational high school. He said that he liked mathematics and science, and expressed some interest in going on to college.

Neurological Evaluation

Dr. Robert Soll:*

This patient's convulsive disorder would be classified in the group known as idiopathic or essential epilepsy in contrast to the symptomatic type in which the cause is known. Although it is now believed that a genetic or hereditary factor is present in all forms of epilepsy, a significantly higher incidence of seizures occurs in families of patients with idiopathic epilepsy. This patient and his siblings demonstrate a typical example of this correlation. The prevalence of affected individuals among parents and siblings of patients with centrencephalic seizures was thirteen per cent compared with only two per cent in the control group.¹

I was impressed with the fact that this patient's convulsive seizures undoubtedly would be well controlled if he took his medications regularly. On the other hand, if his seizures definitely were uncontrolled by medication, a pneumoencephalogram should be considered. In caring for him medically, we may share the blame for his neglect of medications by not having continually attempted to explain the nature of seizures and their treatment. Thus we may have failed to give the patient as complete an insight into his disability as may have been possible. Also there is a marked variability in patients, and both their personality and intelligence may profoundly affect their response to treatment.

Psychological Evaluation

Mr. William Gayton:**

In the light of the patient's medical history we felt that an evaluation in the areas of intelligence, cerebral dysfunctioning and personality would help delineate the factors involved.

Intelligence

Intellectual estimates were obtained from the Binet Vocabulary and the Porteus

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**Clinical Psychology Trainee, University of Minnesota Hospitals.

Mazes. The patient obtained an I.Q. of 88 on the Binet Vocabulary and a I.Q. of 114 on the Porteus Mazes. The Binet estimate is primarily a verbal measure of abstract and conceptual abilities. Therefore, his score places him in the low average range of intellectual functioning. The estimate from the Porteus Mazes indicates that his foresight and planning abilities are slightly above average. These results suggest that in the practical applications of intelligence the patient could be expected to do quite well; however, he would be somewhat limited in abstract thinking or in the tasks that call for complicated reasoning. Plans for a college education should be altered on the basis of such results. Although he should do fairly well in a vocational type setting, I have serious doubts as to his ability to achieve in a college setting.

The patient was given the Graham Kendall Memory For Designs in order to assess those behaviors related to cerebral dysfunctioning. He achieved a perfect score on this instrument which indicates that he has no problems in short-term memory or in the ability to integrate perceptual-motor activities.

The patient's MMPI profile is mild to moderately abnormal. It suggests the presence of acute anxiety and considerable emotional turmoil. There is also a certain amount of depression, social introversion, and social withdrawal. He appears to be a passive, immature individual with rather poor ego strength. Since he tends to be somewhat sensitive and suspicious of the motives of others, he could be very difficult to manage if he thought that others were trying to manipulate him. Some of these behaviors may be related more to situational factors than to internal conflict.

Dr. Soll:

Do you feel that the internal conflict suggested by the MMPI is significant enough to be evaluated further psychiatrically?

Mr. Gayton:

Yes, I think a psychiatric interview in regard to his present emotional functioning would be helpful if he is having problems that he isn't disclosing.

Social Service Evaluation

Miss Helen Kretchmer:*

We often have an opportunity to talk to other members of a patient's family, but in this case we do not. Since the patient has been living in Minneapolis for almost one and one-half years, he came to the University Hospitals unaccompanied by other members of his family. He is a nice-looking, pleasant young man who gives the impression of having much nervous energy and a need to be constantly active. During the interview he handled any uncomfortable subject by laughing. I believe that he felt grown up and responsible for himself. He appeared to deny any concern that he might have about his seizure condition.

Parental Relations

He readily discussed his father, a man in his early fifties and a publisher of a small-town newspaper. Although his father has diabetes, he has worked long hours. The patient felt that this has been very difficult for his father. Very little was said about his mother.

There are five siblings, two of whom are still at home. An older brother, who has had two years at Mankato State College, works at the postoffice in the Cities. His older sister also attended Mankato State College, the University of Minnesota and the University of California. She is married and has two children. In her

*Supervisor, Social Service Department, University of Minnesota Hospitals.

Continued

spare time she does tutoring. Another older brother who is in the army now has had three years of college. Thus one can understand why this young man is considering the possibility of going on to college.

Since the age of 10, the patient has operated his father's presses for the newspaper. At the age of 16 he persuaded his father to buy a \$5,000 German press. When the man came from Germany to instruct them concerning its operation, the father was too busy; so the patient learned the details. Since the father still hasn't learned to operate the press, the patient goes home almost every weekend to help his father. A certain amount of pressure was involved because payments on the press had to be made. At the present time the patient is teaching his 15-year-old brother how to operate the press.

Work Schedule

The patient obtained his present job at an electronics firm last March, 1966, and has just now started working full time. While at the vocational school he was working for this firm a few hours a day. Now he has long working days every day of the week, besides going home to work weekends for his father.

The patient's hobby is hunting. His future plans are to work for a while on his present job and then leave for Alaska with a friend. As far as finances are concerned, the patient has been paying his own way for several years. I was rather interested in the fact that he felt responsible for the bill which was incurred by him for his medical evaluation in 1962.

His vocational high school counselor has advised him to pursue an electronics career. Apparently he was a D student in theoretical courses but averaged C or above in the laboratory courses. His Strong Interest Test indicated him to be high in mathematics and science. Although he was rated as having a somewhat low I.Q. in high school, he was in the middle half of the class on the Air Force test, scoring an 85. The vocational high school training was provided free of tuition. His own instructor said that he generally was a good worker and compared well with others. No real problems existed during his vocational training; however, he was satisfied with less than a good performance at times. The patient had told his instructor that he had a seizure problem. In retrospect, he may have been having more problems than he was aware of. On occasion the instructor drew a blank response from him when he seemed to have forgotten everything that he knew. At other times he appeared groggy or sleepy. These episodes would pass, however, and he would be all right again.

When the patient was still in high school, he purchased a new car. Later he completely demolished it in an accident while driving back from Canada, and now he cannot afford to drive, probably because he still owes money on the car. He would like to be in the Army—even if it were only on limited service. He felt that it would be an interesting experience.

He admitted that he forgets to take his medication at times but said that he would try to do better. Outwardly the patient manifests some of the anxieties that persons with seizures often have. As stated earlier he should have better awareness and better understanding of his condition in order to recognize his need for continued care. Very likely he is unable to foresee now the types of problems that may arise in the future.

Dr. Soll:

Your description of the patient appears to be one of a reliable individual who has helped his parents and has become quite independent. His seizures may repre-

sent to him an obstacle which detracts from his self reliance. In this light he probably dislikes being dependent upon his anticonvulsant medications.

Mr. Gayton:

It is a very interesting possibility that his self concept cannot accept the idea that he has to be dependent upon something in order to function adequately. The drugs themselves can be a sign of weakness to some people.

Dr. Soll:

The fact that he recently requested a statement concerning his health which would permit him to obtain a drivers' license shows a considerable lack of insight by him into his seizures.*

One way of managing this patient would be to see him frequently in order to give him the supportive care, understanding and reassurance that he needs. This could be accomplished by clinic visits at least every two weeks for a few months. In this way he could develop confidence in us. If he has other problems he may then be able to discuss them more readily also.

Voice:

Should a patient have told his employer that he has a seizure disorder?

Dr. Soll:

This has to be the patient's decision. Unfortunately, many employers are unwilling to accept a person who has seizures, particularly when other people who do not have seizures are readily available for jobs.

Miss Kretchmer:

I assume that the patient is an excellent worker. There should be a considerable opportunity for him almost anywhere. Sometimes an employer will overlook quite a lot if one is a good worker.

Conference Recommendations

1. The patient should be seen in clinic at frequent intervals in order to develop a better understanding of his condition and to promote reliability in taking his medications. Visits every two weeks are recommended.
2. A psychiatric referral should be made for the purpose of evaluating further possible emotional conflicts the patient might be having.
3. Any recommendations regarding a college education should be deferred temporarily. More intensive psychological studies may be undertaken if the patient eventually considers college seriously.

Robert Soll, M.D.
University of Minnesota Hospitals

*The state law requires that a patient be seizure-free for two years before being allowed to obtain a driver's license.

Participating in the conference were: Dr. Robert Soll, Neurologist; Miss Helen Kretchmer, Supervisor, Social Service Department; Student Doctor Todd Davis, and Mr. William Gayton, Clinical Psychology Trainee.

Reference

1. Metrakos, J. D., and Metrakos, K., Genetics of Convulsive Disorders: I. Introduction Problems, Methods and Baselines. *Neurology* 10:228, 1960.

Obesity

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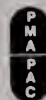
—Helen Rowland

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The Physician's Workshop

Lupus Erythematosus Cell (LE-Cell) Test without A Blood Clot

MANY TECHNIQUES have been devised for the demonstration of the lupus erythematosus cell (LE-Cell) since Hargraves, Richmond, and Morton¹ reported the presence of amorphous cytoplasmic inclusion bodies in leukocytes in the bone marrow of patients with systemic lupus erythematosus.

The Blood Clot Technique

The most widely used tests are the blood clot tests of Zimmer and Hargraves,² and Magath and Winkle,³ which often produce "pseudo lupus erythematosus cells." But these may be difficult to separate from true lupus erythematosus cells by an occasional observer. Thus a lupus erythematosus clot preparation may be reported positive when actually negative. Further, lupus erythematosus clot tests may vary from positive to negative over a period of twenty-four hours.

The Heparinized Blood Technique

Zinkham and Conley⁴ showed that in-vitro lupus erythematosus cell production depends upon three factors: (a) actively phagocytic leukocytes, (b) amorphous nuclear leukocyte material, and (c) the presence of the lupus erythematosus factor. They devised a glass bead-rotary method which gives reproducible results. By traumatizing nonviable leukocytes high yields of amorphous material and lupus erythematosus cells are obtained. Further, their technique produces lupus erythematosus cells when the blood clot tests are negative.

Briefly the Zinkham-Conley technique is as follows: Heparinized venous blood is allowed to stand for two hours; transferred to a flask containing 15 glass beads 4 mm. in diameter, and placed on a rotator for 30 minutes. About 1 ml. of the blood sample is transferred to a Wintrobe hematocrit and centrifuged for 10 minutes at 1,000 r.p.m. Several smears are made from the buffy coat, allowed to air dry for one to two hours, and then stained with Wright's blood stain.

The increasing use by clinicians of the lupus erythematosus cell test has created a problem in many medical laboratories because of the 3½ to four hours necessary to complete the Zinkham-Conley procedure. We have worked out a modification of their technique, reducing the time to 1½ hours. The test retains the high degree of sensitivity yield of amorphous material, lupus erythematosus cells, leukocyte rosettes, and clearance of cellular morphology of the Zinkham-Conley technique. Production of pseudo lupus erythematosus cells is practically nil.

Method

Draw 5 to 7 ml. venous blood into a heparinized 10 ml. B-D Vacutainer tube, invert several times and place 10 glass beads 6 mm. in diameter in the tube. Secure the tube on a rotator and allow to revolve at 25 r.p.m. for 30 minutes. Let stand at room temperature for 30 minutes. Invert the tube several times and centrifuge at

Continued

1,000 r.p.m. for five minutes.

With a Wintrobe pipette remove some plasma and place it in a small test tube. Leave enough plasma over the leukocyte concentrate to permit easy skimming of the buffy layer including a small amount of the uppermost layer of erythrocytes, since lupus erythematosus cells tend to settle at the bottom of the leukocyte column. Expel the sample onto a paraffin-coated watchglass and mix the specimen well with a thin glass rod or a Wintrobe pipette. If the sample is too concentrated, dilute with the spare plasma.

Place a small drop of the specimen on a clean microslide and spread it out to blood smear thickness. Make three smears. Whip rapidly through the air. When dry apply Wright's blood stain for three minutes. Add enough distilled water short of overflow, and mix well by placing a wooden applicator on one end of the slide. Move the applicator up and down on the stain surface for several seconds. Allow the stain to act for five minutes. Rinse with distilled water, and dip the slide into a decolorizer for five seconds (methyl alcohol 5 ml., acetone C.P., 0.5 ml., distilled water 100 ml.). Wash the slide with distilled water and permit it to air dry. Place immersion oil on the smear and press a coverslip over the oil. Survey the smear with the high dry objective beginning at the edges of the smear. The test is positive when only one typical lupus erythematosus cell is observed.

Discussion

According to Dubois⁵ the lupus erythematosus cell test is the mainstay for the diagnosis of systemic lupus erythematosus regardless of the advances made in anti-nuclear antibody tests. While nuclear material of nonviable leukocytes is the source of the amorphous matter present in the lupus erythematosus cell, the process of being phagocytotic seems to depend upon its physical-chemical properties. Dubois, using the heparin, glass bead-rotary technique on 502 proven cases of systemic lupus erythematosus, found 23 per cent had amorphous material only. While it appears that the lupus erythematosus cell factor is an antibody reacting with desoxyribonucleoprotein (DNP) of degenerated leukocyte nuclear material, McDuffie⁶ states that "not all patients with positive lupus erythematosus clot tests have a detectable anti-DNP in their sera. Whether the fact that not all patients with an anti-DNP give a positive lupus erythematosus clot test is due to quantitative differences in the amount of antibody present or to other factors is not known." That the lupus erythematosus cell factor is active in vivo was shown by Schleicher.⁷

In our hands the Zinkham-Conley technique proved superior to the lupus erythematosus clot tests and the results closely correlated with the clinical manifestations of lupus erythematosus. These observations dovetail with those of Dubois,⁵ with whom we agree⁸ that the most characteristic lupus erythematosus cell is found in preparations made from heparinized blood processed by the glass bead-rotary technique.

Conclusion

A routine test to demonstrate the lupus erythematosus cell is presented. The method takes 1½ hours to complete. The test yields amorphous material, lupus erythematosus cells, leukocyte rosettes, and clearness of cellular morphology.

Emil Maro Schleicher, Ph.D.*
Minneapolis, Minnesota

*Director Hematology Section Department of Pathology and Clinical Laboratories, St. Barnabas Hospital, Minneapolis, Minnesota.

Acknowledgment

Thanks are extended for technical assistance to Mrs. Mary E. Lies, Mrs. Linda Ask, Mrs. Nancy Tieglund, and Mrs. Mary E. Afford.

References

1. Hargraves, M. M., Richmond, H., and Morton, R.: Presentation of Two Bone Marrow Elements: The "Tart" Cell and the "L.E." Cell. *Proc Mayo Clin* 23:25, 1948.
2. Zimmer, F. E., and Hargraves, M. M.: The Effect of Blood Coagulation on L.E. Cell Formation. *Proc Mayo Clin* 27:424, 1952.
3. Magath, W. H., and Winke, V.: Technique for Demonstrating "L.E." (Lupus Erythematosus) Cells in Blood. *Amer J Clin Path* 22:586, 1952.
4. Zinkman, W. H., and Conley, C. L.: Some Factors Influencing the Formation of L.E. Cells. *Bull Hopkins Hosp* 98:102, 1956.
5. Dubois, E. L.: *Lupus Erythematosus*. New York, McGraw-Hill Book Company, 1966.
6. McDuffie, F. C.: Anti-Nuclear Antibodies in Various Diseases. *Minnesota Med* 49:1565, 1967.
7. Schleicher, E. M.: "L.E." Cells in Sections of Marrow Units. *Acta Haemat* 10:337, 1953.
8. Dubois, E. L.: L. E. Cell Test and Antinuclear Antibodies. *JAMA* 200:1035, 1967.

Professional Courtesy**Adopted by Judicial Council***

The following guidelines are offered as suggestions to aid physicians in resolving questions related to professional courtesy.

1. Where professional courtesy is offered by a physician but the recipient of services insists upon payment, the physician need not be embarrassed to accept a fee for his services.

2. Professional courtesy is a tradition that applies solely to the relationship that exists among physicians. If a physician or his dependents have insurance providing benefits for medical or surgical care, a physician who renders such service may accept the insurance benefits without violating the traditional ethical practice of physicians caring for the medical needs of colleagues and their dependents without charge.

3. In the situation where a physician is called upon to render services to other physicians or their immediate families with such frequency as to involve a significant proportion of his professional time, or in cases of long-term extended treatment, fees may be charged on an adjusted basis so as not to impose an unreasonable burden upon the physician rendering services.

4. Professional courtesy should always be extended without qualification to the physician in financial hardship, and to members of his immediate family who are dependent upon him.

*American Medical Association, July 17, 1967.

Monkeys are superior to men in this: when a monkey looks into a mirror, he sees a monkey.—Chazal

*In nature there are neither rewards nor punishments; there are consequences.
—Ingersoll*

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The Anemias

THALASSEMIA MAJOR (also called Cooley's, Mediterranean, and erythroblastic anemia) is a hereditary disease in which decreased amounts of heme and globin are synthesized, so that the erythrocytes are microcytic and hypochromic. The erythrocytes, which are not produced at a normal rate, are destroyed prematurely by the reticuloendothelial system, and anemia results. The skeletal changes are due to accelerated hematopoiesis, which causes exuberant growth of the marrow. The earliest changes occur after the first year of life and are seen in the small bones, especially the metacarpals and the metatarsals. In later childhood and early adulthood, the active red marrow tends to recede toward the trunk, and hypoplastic yellow (fatty) marrow is left peripherally, so that the early changes in the distal parts of the tubular bones disappear. At this stage the skull, spinal column, and pelvis tend to show the greatest change. Skull changes are more common and more striking in thalassemia than in any of the other anemias. The diploe is widened; the outer table is displaced outward, and it is often thinned

(Figure 1). The diploic trabeculae may become perpendicular to the tables, and this produces the so-called hair-on-end appearance. The occipital squamosa is always spared inferior to the internal occipital protuberance, presumably because of the normal lack of red marrow in this region (Figure 1). Overgrowth of marrow in the maxillary, sphenoidal, and temporal bones may inhibit pneumatization of the paranasal sinuses and mastoids. Roentgenologically, this is most evident in the maxillary antra. This finding is almost exclusive to thalassemia, and therefore when it is encountered in association with the previously mentioned changes it is virtually pathognomonic. Swelling of the maxillae occasionally displaces the orbits laterally and causes ocular hypertelorism. The tubular bones show coarse trabeculation (chiefly as a result of destruction of the finer trabeculae), pressure atrophy of the cortices, and swelling of the shafts which gives the bones a squared-off appearance (Figure 2). The spinal column may show reticulation and some osteoporosis, but the cupping and compression of the vertebral bodies that are features of sickle-cell anemia do not occur.

Sickle-cell anemia too is characterized by abnormal erythrocytes that are lysed prematurely.

Continued

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The bone lesions are due in part to hyperplasia of the marrow and in part to infarction of bone. Although diploic widening in the calvarium occurs, radial spiculation is rare. In the long bones the medullary spaces are widened and the cortices are thinned. Coarse trabeculation is often seen.

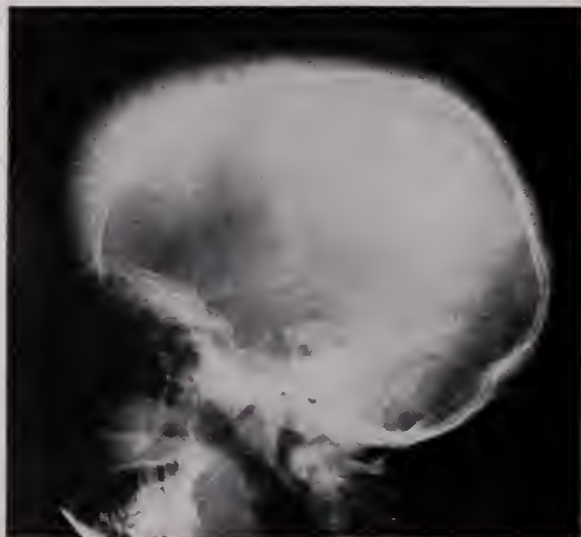


Fig. 1—Thalassemia major. The diploe is markedly widened, and there is radial spiculation. The squamosa below the occipital protuberance is characteristically spared.

An important finding is demineralization of the spinal column. This may be found even in children; in older individuals it often leads to biconcave compression of the vertebral bodies. Moseley¹ contended that the discovery of osteoporosis of the spinal column together with bone infarction and cortical thickening is virtually diagnostic of sickle-cell disease. Infarction of bone in children may cause periosteal thickening or elevation, or there may be frank infarctive changes in the shafts, especially at the ends. Occasionally there is massive infarction of a long bone, suggesting osteomyelitis from a roentgenologic point of view. Gangrene not uncommonly results. In adults, infarction tends to involve the ends of long bones or localized areas in the medulla. The femoral head and less often the humeral head may collapse after infarction. The change seen in the femoral head is indistinguishable roentgenologically from aseptic necrosis due to other causes.

Congenital spherocytosis is a hereditary hemolytic anemia in which spherocytes appear in the peripheral blood. Splenectomy cures the hemolytic process. The roentgen manifestations depend on the same mechanism as in Cooley's anemia—marrow hyperplasia—but the anemia is



Fig. 2—Thalassemia major. The trabecular pattern is coarse, the cortices are thinned, and there is slight squaring-off of the bones.

usually not as severe in hereditary spherocytosis, and the disease usually becomes overt later in life when the peripheral portion of the skeleton is no longer involved in erythropoiesis. Consequently, bone changes are not common, and changes in the tubular bones are distinctly uncommon. When changes are encountered, these are usually in the skull. They are similar to the changes in thalassemia, but less extensive.

Other congenital hemolytic anemias, including hereditary elliptocytosis and the various enzyme abnormality states such as pyruvate kinase deficiency, may cause changes in the calvarium. Iron-deficiency anemia was reported for the first time in 1958² to be a cause of these skull changes, occasionally with radial spiculation. Curiously, the severity of the bone changes apparently does not correlate with the severity of the anemia. No changes have been described in other parts of the skeleton. Recently, secondary polycythemia due to congenital heart disease has been recognized as a cause of similar skull changes.

The Fanconi syndrome consists of anemia, leukopenia, thrombocytopenia, and a series of inconstant congenital defects, the most common of which are hypoplasia or aplasia of the thumb and first metacarpal bones, syndactylism, microcephaly, and ectopia of the external auditory canals. There is nothing diagnostic about these findings, but their presence may serve to suggest the diagnosis in an anemic child. This syndrome is not to be confused with another Fanconi syndrome consisting of cystinosis and refractory rickets.

Leukemia

The incidence of roentgenologically demonstrable bone lesions in childhood leukemia is usually stated to be between 50 and 75%. In adult leukemia it is generally held to be less than 10%, although in the series studied by Silverstein and Kelly³ it was higher. It is notable that the incidence of bone changes is higher in children because their entire marrow space is occupied by blood-forming tissue, so that there is little room for the proliferating leukemic cells, which soon encroach on the bone itself. Adult marrow, being largely fatty, can absorb a large mass of leukemic tissue before the bone itself is destroyed.

The atypicality of the clinical course in children, especially the frequently deceptive onset, makes any aid to diagnosis of more than just academic interest. Leukemia in childhood often

presents with joint pain and even swelling and tenderness, so that the initial diagnosis is often rheumatic fever or juvenile rheumatoid arthritis. The early blood picture frequently shows a normal white cell count, and indeed the white cells may even be diminished in number. Thus, the roentgen findings may be the first indication of the true nature of the disease. These findings in the child will be discussed first.

The roentgen signs of leukemia are (1) the transverse metaphyseal line, (2) osteolytic lesions, and (3) periosteal lesions. The most common and perhaps the most useful sign is the transverse metaphyseal line (Figure 3-A). This line occurs in the metaphysis adjacent to the epiphyseal plate. It tends to be thin and usually extends right across the bone from cortex to cortex, although in some early cases the line is incomplete. It is most often encountered at the knee, although it may be seen in any of the long bones when rapid growth is taking place and even in certain flat bones such as the ilium, just beneath the cortex. The pathologic basis for this finding

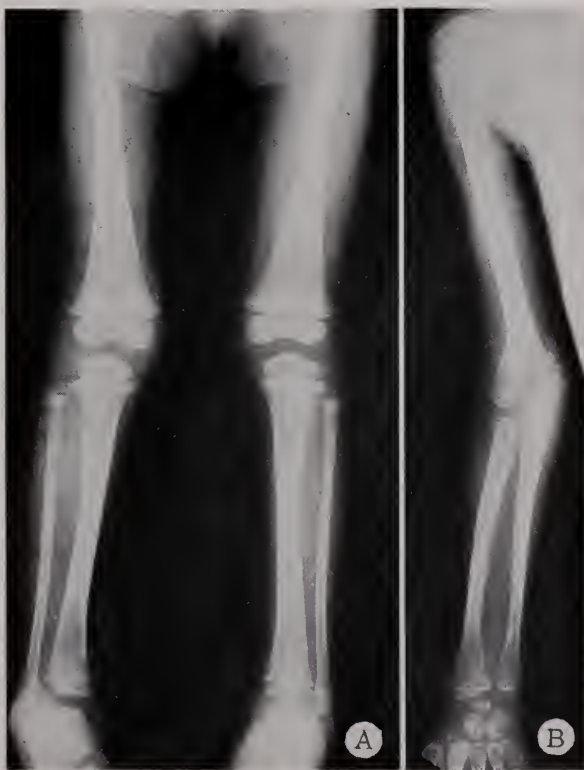


Fig. 3— (A) Childhood leukemia. Note the transverse metaphyseal lines at the knees and ankles. (B) Leukemia in another child. Periosteal reaction is seen along the humeral shaft, and osteolytic lesions are present in all of the bones.

Continued

is not clear, but it may be due to a failure of new enchondral bone formation secondary to the child's poor general health. Microscopic examination of this line has failed to demonstrate leukemic infiltration as the cause. The line is not specific for leukemia, for it is occasionally seen in children with metastatic neuroblastoma, scurvy, syphilis, or acute infections and, though rarely, in apparently normal children. When seen, however, it should alert the clinician to the probability of leukemia.

Osteolytic lesions are the most common finding in childhood leukemia (Figure 3-B). These may present as extensions of the transverse metaphyseal line or may originate *de novo*. The spongiosa is usually affected, but in the early case the cortex is generally spared. Eventually the entire shaft becomes involved, and generalized demineralization occurs. The cortex may show areas of destruction, most often in the long bones but also in the skull and pelvis. In the skull increased intracranial pressure may be seen with decalcification of the sella and spreading of the sutures. There is often an apparent coarsening of the trabeculae of long bones due to destruction of the finer trabeculae. This is accentuated by the destruction of the overlying cortex. Instead of regions of osteolysis, there may be a generalized demineralization.

Periosteal changes are quite common, and they are the usual cause of limb pain (Figure 3-B). These changes are caused by the proliferation of leukemic cells between the cortex and the periosteum, the result being elevation of the periosteum and sometimes periosteal new bone formation. Despite the tendency of leukemic patients to hemorrhage, it is uncommon for the periosteal elevation to be due to bleeding. This process occurs most often in long bones, but it is also seen in the short tubular bones of the hand and foot and in the ribs.

In the adult the same findings described for childhood leukemia are seen, although far less often. The very useful sign of the translucent metaphyseal line is rarely seen in the adult. The differential diagnosis of skeletal involvement in leukemia should include consideration of metastatic neuroblastoma, malignant lymphoma, and juvenile rheumatoid arthritis. Metastatic neuroblastoma and lymphoma may actually be quite indistinguishable from leukemia.

Myelosclerosis

Myelosclerosis, a blood disorder of middle and late life, is characterized by fibrotic or sclerotic changes in the bone marrow, marked splenomegaly, and often hepatomegaly. It is sometimes superimposed on long-standing polycythemia rubra vera. Of the many synonyms for this disease, the most common are myelofibrosis and agnogenic myeloid metaplasia with myelofibrosis. Perhaps the term "myelosclerosis" should be reserved for cases involving increased bone density. Early in the disease the marrow is hyperplastic, having a moist, red, succulent appearance. Later, marrow atrophy dominates, and fibrous tissue replaces the marrow; eventually this fibrous tissue calcifies. In effect, there are encroachment of the spongiosa on the marrow space and progressive obliteration of the marrow. The trabeculae become increased both in number and in thickness.

In one third to one half of all cases there are roentgenologically demonstrable bone changes. Tutton⁴ concluded that two kinds of bone change were present. The first, and more common of the two, consists of increased bone density (Figure 4). The second combines increased density with a large number of radiolucent areas (Figure 5). The first form consists of a spectrum from a slight increase to a marked increase in density in which the trabecular pattern is no longer discernible. The contour of the bones is not affected, and the involvement is rather homogeneous except for the greater involvement of the central portion of the skeleton. Extensive involvement distal to the elbow or the knee is distinctly uncommon. In mild cases the cortical-cancellous differential is present but reduced; in advanced cases it may be lost. This change is best appreciated in the medial ends of the clavicles and in the ribs.

The second type of bone change combines the features just mentioned with numerous radiolucencies which are usually elliptical and which measure 2 mm. by 3 or 4 mm. A finding that may be confusing is that the trabecular pattern is actually more distinct than it is normally in the upper part of the femora and the humeri and in the superior part of the acetabula. There are no skip areas that are spared by the lytic lesions, so that if one area of the central skeleton is involved, the entire central skeleton is involved. These lytic areas are probably due to fibrous tissue proliferation and islands of hematopoiesis.



Fig. 4—Myelosclerosis of the sclerotic type. (From Pugh, D. G.: *Roentgenologic Diagnosis of Diseases of Bones*. Baltimore, Williams & Wilkins Company, 1951, p. 484. By permission of Williams & Wilkins Company.)



Fig. 5—Myelosclerosis of the combined lytic and sclerotic type. The appearance of the ribs is not unlike that sometimes seen in myeloma and metastatic carcinoma. Compare with Figure 4.

Because the changes are most extensive in the central portion of the skeleton, the diagnosis is often suggested on chest or abdominal roentgenograms, especially if an enlarged spleen is seen.

Myelosclerosis must be distinguished from osteopetrosis, osteoblastic metastases, fluoride osteosclerosis, urticaria pigmentosa, multiple myeloma, and Paget's disease. If more than a localized area of the skeleton is examined, there should rarely be any difficulty in distinguishing these diseases from myelosclerosis.

Osteopetrosis is a disease of children who rarely survive into adulthood; therefore this diagnosis in an adult should be highly suspect. It is characterized by a general increase in bone density with loss of the internal roentgen anatomy of the bone, so that the cortex, medullary cavity, and epiphyseal plates are obliterated. The ends of long bones are often clubbed, and there may be transverse or longitudinal striations in the bones. The vertebral bodies have a characteristic appearance in the lateral view, namely dense superior and inferior plates with a normal-appearing centrum.

Osteoblastic metastases (usually prostatic) are rarely distributed so evenly as to cause difficulty in diagnosis. On a single film, myelosclerosis may be simulated, but a bone survey allows the differentiation to be made easily.

Fluoride poisoning is encountered in several well-known regions of the country. Also, there is often ligamentous calcification in the pelvis; and splenomegaly does not occur.

Urticaria pigmentosa is distinguished on the basis of the clinical and laboratory data.

Multiple myeloma may give the appearance of the mixed type of myelosclerosis, but in myeloma the bone density is not increased, pathologic fractures occur (they do not in myelosclerosis), and the spleen is not enlarged.

Paget's disease rarely causes difficulty, for the trabecular pattern, the expansion of bone, and the limited skeletal involvement are all characteristic of the disease.

Urticaria Pigmentosa

Urticaria pigmentosa, or mastocytosis, is an uncommon disease which has been receiving the attention of roentgenologists for only a few years (Figure 6). It is a systemic malady which always involves the skin and frequently involves the bone marrow, lymph nodes, and viscera. Clini-

Continued

cally it is characterized by skin pigmentation that urticates readily, so that dermatographia is possible. Large deposits of mast cells are present in the involved tissues, and their high histamine content is presumably responsible for the urtication. Sagher and associates⁵ first reported bone changes in urticaria pigmentosa in 1952. Stark and co-workers⁶ were the first to correlate the roentgen changes and microscopy. They showed that there are areas of bone marrow replacement by dense aggregates of mast cells and associated areas of reactive new bone formation. Sagher and Schorr⁷ established a central registry for the collection of the roentgen manifestations of the disease, and from this they concluded that the bony lesions were of two types—localized and generalized. However, none of the localized lesions were subject to biopsy, and the findings were rather vague; for the present, therefore, it is probably best to consider only the generalized type of bone changes.

These changes consist of generalized cystic osteoporosis of the ribs, thickened bony trabeculae, cranial stippling, and thickening of the tables of the skull and generalized sclerosis of the vertebrae and pelvic bones. In some cases roentgen examination of the gastrointestinal tract reveals diffuse mucosal changes due to infiltration by mast cells.

Multiple Myeloma

Multiple myeloma is characterized by malignant proliferations of plasma cells. Two forms have been recognized—solitary and multiple—but, given time, the solitary form usually matures into multiple myeloma. The clinical manifestations of multiple myeloma are protean and well known and need not be repeated here. It should be emphasized that intravenous excretory urography is contraindicated in myeloma, for this procedure often precipitates acute renal failure.

Roentgenologic bone changes are present in 75 to 95% of cases of myeloma. Classically one encounters "punched out" areas of bony destruction (Figure 7), which are best seen in the skull. These may occur in any bone, although they are rarely seen in the vertebrae. There is virtually never any bony condensation at the margins of these lesions (Figure 7), and the trabecular structure is completely destroyed. Lytic metastases are rarely as well circumscribed as the punched-out lesions of myeloma are. Another helpful point of



Fig. 6—Urticaria pigmentosa. Note the resemblance of the ribs to those in Figure 5. There are also changes in the left humerus and scapula.



Fig. 7—Multiple myeloma. There are characteristic "punched out" lesions in the pelvis and expanding lesions in many of the ribs. Note the absence of marginal sclerosis. (From Pugh, D. C.: *Roentgenologic Diagnosis of Diseases of Bones*, Baltimore, Williams & Wilkins Company, 1951, p. 488. By permission of Williams & Wilkins Company.)

distinction is that occasionally there is an associated soft-tissue mass in myeloma, especially adjacent to the ribs; this almost never occurs in metastatic bone disease. Quite often, involved ribs are expanded, and in the absence of a soft-tissue mass, the differential diagnosis must include fibrous dysplasia, hyperparathyroidism, metastases, aneurysmal bone cyst, and histiocytosis X. When a soft-tissue mass is present, the differential diagnosis is between myeloma and primary malignant disease of the rib such as Ewing's sarcoma, chondrosarcoma, and reticulum cell sarcoma.

In other areas of the skeleton, hyperparathyroidism may be simulated, although subperiosteal resorption of bone never occurs in myeloma. The bone lesions of myeloma tend to cause pathologic fractures, especially of ribs and vertebrae. Pugh⁸ has pointed out that in metastatic bone disease involving the head, the mandible is usually spared.

In myeloma, on the other hand, the calvarium and the mandible may be involved equally.

A very important and rather constant finding is demineralization, which may be generalized or may be localized to the spinal column. Demineralization occurs when there is generalized involvement of the marrow without the formation of discrete tumefactions or plasmacytomas. The myeloma tissue thins the cortex and reduces the trabeculae in both thickness and number. Vertebral body collapse is often encountered. The presence of an associated soft-tissue mass adjacent to the spinal column favors myeloma over metastasis, but it does not rule out lymphoma.

Myeloma may, like metastatic hypernephroma and thyroid carcinoma, cause large areas of bone destruction with no sclerosis, especially in the pelvis. In the sacrum this change may be difficult to see, because of thinness of the bone and overlying gas.



Fig. 8—(A) Anteroposterior and (B) lateral views of the knee of a boy with hemophilia. The epiphyses are abnormally large and radiolucent. On the original roentgenograms, deposits of hemosiderin were evident in the soft tissues around the joint.

Continued

Lymphoma

Primary lymphoma of bone has come to be recognized as a real although uncommon entity which afflicts patients usually in the third to fifth decades. The lesions, which have a predilection for the long bones, typically start at the end of the bone. They often progress to involve a long segment of the shaft. The roentgen appearance is usually not diagnostic, although it almost always suggests the presence of a malignant bone tumor. Characteristically there is extensive disruption of the bony architecture, frequently with a mixture of lysis and sclerosis that results in a moth-eaten appearance. There is usually no periosteal reaction. An associated soft-tissue mass is common and, when present, aids in arriving at the correct diagnosis. The soft-tissue mass may contain calcification. Occasionally, lymphoma will involve bones on both sides of a joint. This may

rarely occur in myeloma and in infection. Other lesions that must be distinguished are osteogenic sarcoma, Ewing's sarcoma, and metastasis. Secondary deposits of lymphoma in bone may be either osteolytic or osteoblastic, and there is nothing about their roentgen appearance that helps in identifying them as lymphoma.

Hemophilia

Hemophilia and Christmas disease are the only bleeding diatheses that commonly cause bleeding of significant degree into bones and joints. Classic hemophilia is more common and more serious than Christmas disease, and it manifests itself most often as joint hemorrhage and occasionally as bleeding into bone itself. The arthritic changes will be considered first. The knee is most often involved, followed in order of frequency by the elbow and the ankle; the shoulder, hip, and wrist

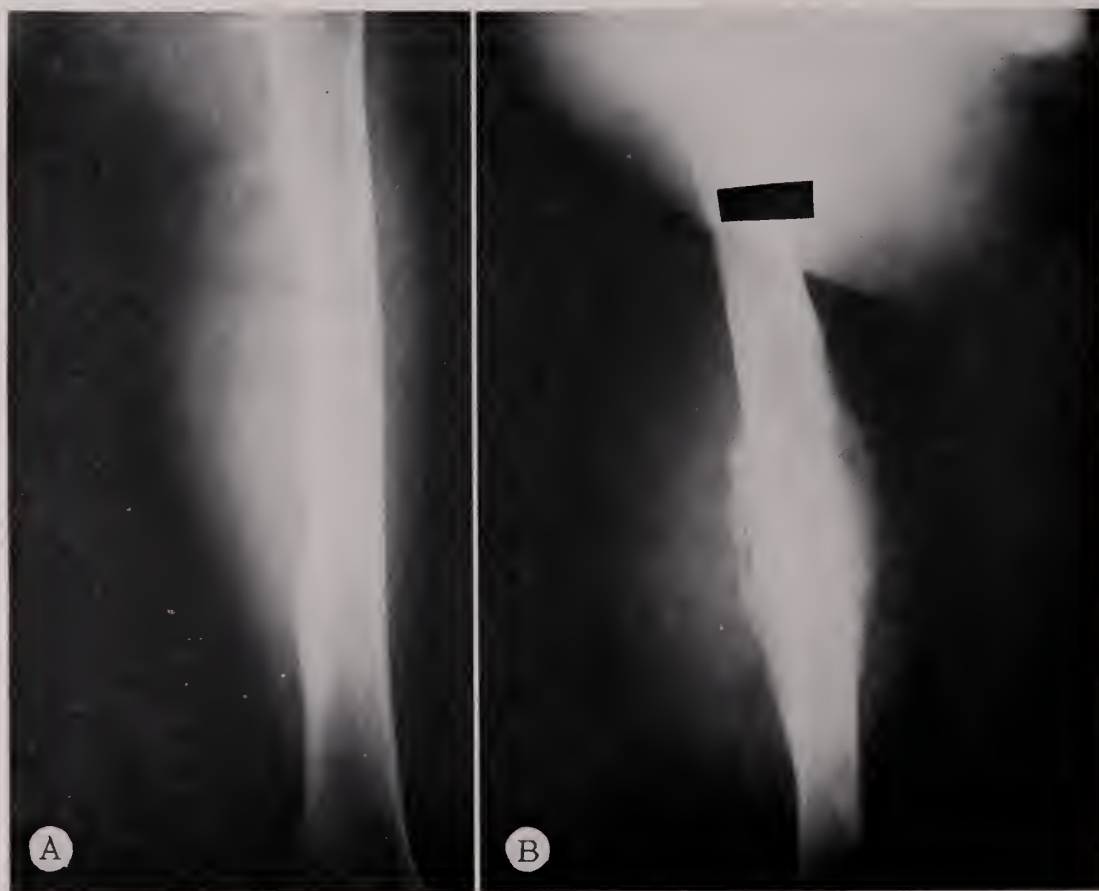


Fig. 9—(A) Anteroposterior and (B) lateral views of the femoral shaft of a patient with hemophilia. There are cortical destruction, new bone formation, and a large soft-tissue mass; hemophilic pseudotumor. (From Ghormley, R. K., and Clegg, R. S.: Bone and Joint Changes in Hemophilia: With Report of Cases of So-called Hemophilic Pseudotumor. *J Bone Joint Surg [Amer]* 30A:589, 1948. By permission of the Journal of Bone and Joint Surgery.)

joints are uncommonly affected. The early stages of hemophilic arthropathy are probably no different from nonhemophilic hemarthrosis. The roentgenologic appearance is of increased density of the periarticular soft tissues and distention of the joint space. After repeated hemorrhages the blood that remains causes a chronic synovitis in which villous hyperplasia of the synovium develops and subsynovial fibrous tissue is laid down. The periarticular soft tissues become thickened, and hemosiderin is deposited in and around the joint; this may be detectable roentgenologically. The attendant hyperemia causes osteoporosis of the surrounding bone, and this may be a striking



Fig. 10—Gaucher's disease with so-called Erlenmeyer-flask deformity of the distal part of the femur. The cortex is thinned, and the medullary cavity is rather radiolucent. (From Pugh, D. G.: *Roentgenologic Diagnosis of Diseases of Bones*, Baltimore, Williams & Wilkins Company, 1951, p. 479. By permission of Williams & Wilkins Company.)

feature. Hyperemia may also cause enlargement and accelerated maturation of the epiphyses with premature fusion (Figure 8). These changes are best appreciated by comparing the affected joint with its unaffected mate. Juvenile rheumatoid arthritis and tuberculous arthritis also cause accelerated epiphyseal growth and maturation, presumably by the same mechanism. A finding, not unique to hemophilia but characteristic of the disease, is widening of the intercondylar notch. This is probably caused by erosion of the bone that is not protected by cartilage.

As a result of encroachment by the hypertrophied synovium, erosion of the articular cartilage occurs (starting at the margins), and there is narrowing of the joint space. Cysts commonly develop in affected joints. These cysts are irregular in both size and distribution, and although subchondral bone cysts are seen in other arthropathies, they are rarely seen in such profusion and with so much variation in size in nonhemophilic arthritides. Whether these cysts are due to hemorrhage into subchondral bone or to degenerative changes in the subchondral bone, as in osteoarthritis, is a moot point. It may well be that both mechanisms obtain. In time, osteophytes form, especially in weight-bearing joints.

Bleeding into bone is much less frequent, but it is often more dangerous than joint bleeding. The hemorrhage may be self-limited and of little significance, or it may be severe enough to kill the patient. When subperiosteal hemorrhage occurs, it usually behaves in the same way as hemorrhage from other causes: the hematoma calcifies, periosteal new bone is laid down, and eventually resorption occurs. In some instances, however, sufficient pressure builds up in the hematoma to erode the underlying cortex, and this, together with the hematoma calcification and periosteal new bone formation where the periosteum is elevated from the cortex, may simulate a malignant tumor, as Ghormley and Clegg⁹ have shown. This lesion, which has been referred to as "hemophilic pseudotumor," is usually found in the femur (Figure 9). Occasionally, when bleeding is into the epiphysis of a weight-bearing joint such as the hip, collapse of the epiphysis may result.

Gaucher's Disease

Gaucher's disease is a reticulosis in which cerebroside are accumulated in the reticuloendothelial system. The affected cells (Gaucher cells) are

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present in the spleen, liver, lymph nodes, bone marrow, and occasionally in other organs. Although most afflicted persons are Jewish, apparently no race is immune. Approximately 70% of patients with Gaucher's disease have bone changes.

The earliest discernible roentgenologic change is a generalized demineralization of the distal part of the femora, with destruction of the spongiosa, due to proliferation of the Gaucher cells. As the disease progresses, the normal concavity of the medial side of the distal portion of the femur is lost, and eventually the border becomes convex. The same change occurs, albeit later, along the lateral border. The femur with advanced changes has been likened to an Erlenmeyer flask (Figure 10). This appearance is not pathognomonic of Gaucher's disease, for it is found in other conditions in which abnormal cells replace the bone marrow and encroach on the cortex. The ends of other long bones may be similarly demineralized and swollen, but usually less strikingly. The

changes are not limited to the metaphyses; the entire shaft may show thinning of the cortex and destruction of trabeculae. The cortex may be scalloped internally or it may be expanded, and the affected medullary regions may show homogeneous rarefaction or they may be coarsely reticulated. Sclerosis is an important feature of Gaucher's disease. This may be a result of a reparative process secondary to the destruction caused by infiltration of the Gaucher cells, although this is not an established fact. A common complication is collapse of the femoral heads as a result of infiltration by the Gaucher cells. The appearance of the collapsed head itself is no different from that in which the collapse is due to other causes, such as sickle-cell disease, caisson disease, cortisonism, and idiopathic avascular necrosis, although the appearance of the femoral shaft may provide a clue to the diagnosis. Occasionally, collapse of the humeral head and of vertebral bodies occurs by the same mechanism.

References

1. Moseley, J. E.: Bone Changes in Hematologic Disorders (Roentgen Aspects). New York, Grune & Stratton, Inc., p. 21, 1963.
2. Lie-Injo, L. E.: Chronic Iron Deficiency Anaemia With Bone Changes Resembling Cooley's Anaemia. *Acta Haemat (Basel)* 19:263, 1958.
3. Silverstein, M. N., and Kelly, P. J.: Leukemia With Osteoarticular Symptoms and Signs. *Ann Intern Med* 59:637, 1963.
4. Tutton, R. H.: The Roentgenographic Findings in Myelosclerosis. (Unpublished data.)
5. Sagher, F., Cohen, C., and Schorr, S.: Concomitant Bone Changes in Urticaria Pigmentosa. *J Invest Derm* 18:425, 1952.
6. Stark, E., Van Buskirk, F. W., and Daly, J. F.: Radiologic and Pathologic Bone Changes Associated With Urticaria Pigmentosa: Report of a Case. *Arch Path (Chicago)* 62:143, 1956.
7. Sagher, F., and Schorr, S.: Preliminary and Short Report: Bone Lesions in Urticaria Pigmentosa: Report of a Central Registry on Skeletal X-ray Survey. *J Invest Derm* 26:431, 1956.
8. Pugh, D. G.: Roentgenologic Diagnosis of Diseases of Bones. Baltimore, Williams & Wilkins Company, p. 490, 1951.
9. Ghormley, R. K., and Clegg, R. S.: Bone and Joint Changes in Hemophilia: With Report of Cases of So-Called Hemophilic Pseudotumor. *J Bone Joint Surg (Amer)* 30A:589, 1948.

I Wanted to Be of Use in The World

In my childhood, doctors always seemed to me the highest type of human beings. They of all people, I thought, must be thoroughly good and constructive: their lives were dedicated to helping human life and comfort. I idolized my two brothers who were doctors, and the old physicians in Lynchburg whom I knew won my devoted respect. Doctor Dulaney and Doctor Latham and every other doctor were living forms of kindness; it seemed to emanate from their eyes, their fingers and their smiles. Knowing these men, I could not ever imagine that there could exist medical men who would quibble over fees, or chase ambulances, or go out to play golf after they had operated on a patient. These old doctors, despite the lack of our modern knowledge, brought profoundly healing self-sacrifice to their work. From the first day that I thought seriously about studying medicine, I held the profession in the highest idealism. To sign over one's life to the dedication of human needs: there could be no finer life to live!

Rosalie Morton (1876-) in *Why We Became Doctors*, edited by Noah Fabricant, 1954.

Untoward Reactions Associated with Antimicrobial Therapy

Part I. Cardiovascular, Respiratory,
Gastrointestinal, Hematopoietic, and
Genitourinary Reactions

ALTHOUGH ANTIMICROBIAL drugs have a welcome and salutary effect on many human infections, they often represent a double-edged sword by producing undesirable effects on the host. Some of the untoward reactions after treatment with these drugs are predictable, in the sense that a given ill effect is known to have an expected rate of occurrence. Contrariwise, other undesirable effects appear to be of increased incidence in certain predisposed subjects and are idiosyncratic and consequently often unpredictable. The purpose of this paper is to outline some of the untoward reactions that may occur after administration of the antimicrobial drugs in common use. An attempt will be made to categorize these reactions according to the various bodily systems or areas involved. Members of our group¹⁻⁷ and others⁸⁻¹³ have periodically reviewed this subject.

Cardiovascular

Pericarditis is a rare manifestation of allergy to a penicillin, and it has occurred also after the use of streptomycin or a tetracycline.

Antibiotic-induced changes in the microflora of the host may contribute to the occurrence of *endocarditis* in postcardiotomy patients, especially when such pathogens as *Candida* or diphtheroids are responsible.

Cardiac arrest may result from the potential curariform action of such drugs as streptomycin, dihydrostreptomycin, neomycin, kanamycin, polymyxin B (Aerosporin), and colistin (Coly-Mycin). Such an effect has occurred on intracavitary instillation of these drugs and should be

considered when they are given intramuscularly or intravenously to certain predisposed patients, as will be noted later. Administration of amphotericin B has resulted in cardiac arrest and arrhythmias including ventricular fibrillation.

Anaphylactic reactions may produce almost all types of cardiac arrhythmias, including various forms of heart block. Whether the reaction contributes to the production of actual myocardial infarction is debatable.

Diffuse vasculitis may be a rare manifestation of penicillin hypersensitivity. Like a number of other drugs, the penicillins appear to precipitate disseminated lupus erythematosus. Use of a sulfonamide also seems to precipitate lupus erythematosus and to result in periarteritis nodosa.

Intravenously administered antibiotics that are commonly responsible for chemical thrombophlebitis at the site of administration include amphotericin B, vancomycin (Vancocin), nafcillin (Unipen), the tetracyclines, ristocetin (Spon-tin), erythromycin, and cephalothin (Keflin). Solutions of sulfonamide salts for parenteral administration, such as sodium sulfadiazine and sulfoxazole, are highly alkaline and irritating to the tissues; if they are permitted to leak from a vein, necrosis of the tissues with sloughing may result. Frequent and repeated intravenous injections of these sulfonamides are not recommended because they tend to produce thrombosis of the veins. Due to the possibility of inducing chemical phlebitis, use of leg veins for introduction of these and other antimicrobial drugs is to be avoided.

In patients with cardiac disease one should be

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aware of the increased intake of sodium on use of such antimicrobial drugs as methicillin, cephalothin, or a parenterally administered sulfonamide. Likewise, one should be aware of the potassium content in penicillin G given to these patients.

A "typhoid shock" syndrome after administration of chloramphenicol (Chloromycetin) to patients with typhoid fever is presumed to be due to excessive release of endotoxin and is similar to so-called bacteremic shock due to other gram-negative bacilli. Hypotension, of course, may be part of an anaphylactic reaction to almost any antimicrobial drug, but may present as an apparently isolated reaction to certain drugs, such as nitrofurantoin (Furadantin) and amphotericin B.

Peripheral vascular collapse may occur as a manifestation of the "gray syndrome," which has been noted in infants treated with chloramphenicol.

Respiratory

Among the manifestations of a reaction of the anaphylactic type, there may occur asthmatic respiration and various degrees of edema, including that of the larynx. The respiratory difficulty may become progressively severe until the subject is entirely preoccupied with breathing. He may recover slowly in the ensuing few minutes, or he may die in convulsions, literally gasping for breath. It is worth noting that in man there is no one dominant "shock organ" involved in anaphylaxis, and bronchospasm is not invariable.

On occasion, certain antimicrobial agents, especially the penicillins and nitrofurantoin, precipitate an isolated episode of asthma.

Use of a penicillin, erythromycin, novobiocin (Albamycin), lincomycin (Lincocin), cephalothin, and other drugs may depress the coccal members of the body flora and encourage superinfection in the form of pneumonia, due to overgrowth of such resistant organisms as *Klebsiella*, *Aerobacter*, *Pseudomonas*, and *Candida*. Periodic examination of the sputum and stools may allow detection of changes in the body flora in time to avert clinical superinfection. Contrariwise, administration of streptomycin, kanamycin, the tetracyclines, and other drugs may depress the gram-negative elements of the normal flora and allow the development of pneumonia because of the overgrowth of resistant staphylococci. Of course, superinfection is not limited to the respira-

tory tree, but can result in enterocolitis, bacteremia, pyelonephritis, and so forth. The phenomenon of superinfection due to antimicrobial-induced changes in the bacterial flora may be noted as early as the fourth or fifth day after therapy is initiated. Cessation of therapy responsible for a change in the bacterial flora is usually followed by a return to a normal flora within days, but in certain patients with diseases characterized by lowered general resistance, such may not occur for several weeks. In general, subjects most susceptible to superinfection appear to be infants, persons with underlying pulmonary disease, patients having a defect in immunizing capacity, and those receiving prolonged, intensive, or combined antimicrobial therapy. Strains of staphylococci, gram-negative bacilli, and yeasts appear to be the most commonly encountered organisms in systemic or visceral superinfections.

Superinfection, especially that due to *Pseudomonas* organisms, may complicate "mist therapy" that employs tap water as a vehicle. Similar infection may occur after tracheostomy because of the presence of "water bacilli" in various fluids and on medical instruments exposed to fluids. As previously noted, superinfection due to these organisms is abetted if the patient is receiving a drug, such as a penicillin, to which these bacilli are resistant; the bacilli are thereby relieved of the tendency to natural eradication by their normal microbial antagonists contained in the bodily flora.

Respiratory arrest may occur after use of the antimicrobial drugs that have a potential curariform action, such as streptomycin, kanamycin, neomycin, polymyxin B, and colistin. As noted in the case of cardiac arrest, a curariform effect is most likely to occur on intracavitary instillation of such drugs; however, intravenous administration of polymyxin B has caused respiratory arrest.¹⁴ Instillation of more than 2 mg. of streptomycin, more than 1 mg. of kanamycin or neomycin, or more than 0.5 mg. of polymyxin B or colistin per kg. of body weight into the pleural or other cavity of the narcotized, anesthetized patient is to be avoided. In the surgical patient, aspiration of the bulk of the solution containing one of these drugs at the end of the operation reduces the hazard of apnea or respiratory distress. Of course, under these circumstances, respiratory arrest is not central in origin but reflects neuromuscular blockade.

When, on occasion, certain antimicrobial drugs are administered as an aerosol, in some subjects the procedure may result in irritation of the bronchial tree. The resulting chemical bronchitis may produce findings that can be confused with those of the underlying respiratory condition.

Intrapleural instillation of various antimicrobial agents may also result in an untoward reaction in the form of chemical irritation. Such a reaction in some cases appears to represent host peculiarity. However, it is generally recommended that one avoid instilling certain drugs, such as the tetracyclines, into the pleural or other body cavity because of their irritating properties.

Pleuropneumonitis may represent an allergic reaction to nitrofurantoin and may be mistaken for other entities. Widespread crepitant or subcrepitant rales may be noted, and roentgenograms of the thorax may be clear or may reveal patchy infiltrations at the bases of the lungs. In patients with organic heart disease, these findings may be interpreted as manifesting pulmonary edema and cardiac failure. Chills, fever, cough, and dyspnea may be suggestive of pneumonia. Eosinophilia is frequent but not characteristic of eosinophilic pneumonitis, and the infiltrates are transient but not migratory.

The observation has been made that nalidixic acid (NegGram) may be capable of decreasing ventilation in patients with respiratory deficit.

Respiratory distress and cyanosis are among the manifestations of the "gray syndrome" which may follow the administration of chloramphenicol to infants. Respiratory distress and cyanosis are also among the multiple untoward reactions that may complicate therapy with amphotericin B.

Gastrointestinal

Glossitis and stomatitis may follow the use of certain antimicrobial drugs, including a penicillin, streptomycin, tetracycline, chloramphenicol, and lincomycin. A tetracycline given to the mother in late pregnancy or to the child during infancy or early childhood may cause subsequent discoloration of the child's teeth.

Any antibacterial agent given orally may cause gastrointestinal irritation, apparently reflecting its chemical nature and the individual's tolerance. The tetracyclines, the semisynthetic antistaphylococcal penicillins, lincomycin, nitrofurantoin, and

the sulfonamides not uncommonly generate such distress. Untoward reactions of this type include anorexia, belching, pyrosis, nausea, vomiting, abdominal cramps, and diarrhea. In this regard, loose stools are noted in about 15% of patients receiving lincomycin by the oral route, and diarrhea has required discontinuation of therapy in 2 to 3%. As a further example, gastrointestinal disturbances after oral administration of nitrofurantoin require discontinuation of its use in about 5% of cases. Of course, when frank diarrhea develops in a patient receiving certain predisposing drugs, a specimen of stool should be examined by smear and culture in an attempt to detect staphylococci. The potentially ominous significance of staphylococcal enterocolitis complicating treatment with tetracyclines, as well as with other agents such as streptomycin and the sulfonamides capable of depressing the normal gram-negative elements of the gastrointestinal flora, is well known. Such superinfection will be elaborated on in a paragraph to follow dealing with the effects of antimicrobial drugs on the normal flora of the gastrointestinal tract. Pruritus ani is particularly likely to be precipitated by oral use of a tetracycline. Proctitis may occur after therapy with a tetracycline, as well as with other drugs, including lincomycin.

Certain antimicrobial drugs, such as the semisynthetic antistaphylococcal penicillins, are not well absorbed after oral administration unless the stomach is otherwise empty. Food interferes with the absorption of these drugs, and consequently the decreased levels in serum may be insufficient to eradicate an infection. In this regard, although penicillin V and phenethicillin are said to be interchangeable for clinical use, the potassium salt of penicillin V has the advantage that its absorption is not similarly reduced.^{15,16}

An untoward reaction to penicillin G rarely has taken the form of hematemesis apparently due to an urticaria-like reaction of the gastric mucosa. Cases of bleeding from the gastrointestinal tract have occurred after ingestion of nalidixic acid. Hemorrhagic gastroenteritis is one of the complications of therapy with amphotericin B. Of course, many of the antimicrobial agents, especially those given orally, may prove sufficiently irritating to provoke an exacerbation of a peptic ulcer, with consequent gastrointestinal bleeding.

Continued

Neomycin administered orally in maximal daily doses may produce malabsorptive effects resembling those found in nontropical sprue. These effects include steatorrhea, azotorrhea, and interference with the absorption of vitamins, sugars, and minerals.

A serious biologic complication of antibacterial therapy in the gastrointestinal tract is the overgrowth of resistant organisms. As intimated under respiratory reactions, the microbial etiology of superinfection depends on the antibacterial spectrum of the agent employed, the endogenous flora of the host, and the organisms indigenous to a given environment. As previously noted, the administration of certain antimicrobial drugs, such as one of the tetracyclines, particularly to postoperative patients, may be associated with enterocolitis due to superinfection with coagulase-positive *Staphylococcus aureus*. This serious complication is not limited to surgical patients, but this is the most common clinical setting. Theoretically, oral use of predisposing antimicrobial drugs, rather than parenteral use, is more likely to cause staphylococcal enterocolitis, since it is difficult to build up a high concentration of an agent in the bowel on parenteral administration. Also, the better an agent is absorbed from the bowel, the less should remain therein to affect the flora, and hence the less the likelihood of staphylococcal superinfection; but again this is theoretic. Among the antibacterials depressing the gram-negative flora and predisposing to staphylococcal enterocolitis are the sulfonamides, streptomycin, neomycin, kanamycin, the tetracyclines, chloramphenicol, polymyxin B, and colistin.

Of course, superinfection is not limited to the intestinal tract and, as aforementioned, may result in pneumonia, bacteremia, pyelonephritis, and so forth. In addition to resistant staphylococci, overgrowth of gram-negative bacilli may occur after administration of a penicillin or an allied drug. Although use of one of the latter drugs may eliminate the coccal elements of the intestinal flora, the overgrowth of the gram-negative bacillary elements usually is not associated with clinical manifestations of an enteric nature. Superinfections with gram-negative rods are frequently due to *Escherichia coli*, *Aerobacter aerogenes*, *Proteus*, and *Pseudomonas*. In some patients, it may be difficult to ascertain whether these gram-negative organisms actually represent superinfec-

tion or whether they were present but masked in the initial infection.

In addition to bacterial superinfections, systemic dissemination of *Candida* may occur.¹⁷ Important diagnostic features may include the development of confusion or coma and hypotension associated with leukocytosis in patients receiving antimicrobial drugs, particularly in combination with adrenocortical steroids or antineoplastic agents.

Theoretically, at least, alterations in the bodily flora associated with the administration of antimicrobial drugs may represent a loss of bacterial function. As an example of this, synthesis of vitamin K, normally a function of the flora of the bowel, may be decreased when the flora is altered by antimicrobial therapy. Therefore, anticoagulants may be relatively more potent, and loss of control of coagulation may ensue with the previously correct dosage of the anticoagulant.

There are indications that administration of a tetracycline, especially intravenously, may interfere with coagulation of blood, via mechanisms other than alteration of the synthesis of vitamin K by the bacterial flora. This effect appears most likely to occur in patients who have had a bleeding tendency. Increased clotting time, decrease in plasma prothrombin activity, inhibition of prothrombin consumption, and retardation of thromboplastin generation are among the defects that may occur. In some of these patients, tetracycline-induced hepatotoxicity may be responsible for faulty coagulation.

The tetracycline group of antibiotics is concentrated in the liver, and these drugs have demonstrated their capability of producing fatty infiltration in the liver of experimental animals and of man.^{2,5,9} In 1951, Lepper reported fatal hepatotoxicity in human subjects after intravenous administration of large doses of a tetracycline. Hepatotoxicity after administration of a tetracycline in usual dosages has been observed during pregnancy, and the use of these drugs should be avoided in pregnant women unless their use is virtually mandatory. In keeping with the available data, it would seem advantageous to utilize the tetracyclines cautiously in patients with underlying liver disease. Other possible factors enhancing the likelihood of a hepatotoxic reaction include a daily dose in excess of 2 Gm., prolonged therapy, associated renal disease (which may result in serum accumulation of the drug),

and concurrent exposure to other hepatotoxic agents. In subjects who are predisposed to tetracycline-induced hepatotoxicity, one should monitor the blood levels; one should lower the dose if the serum concentration of the tetracycline exceeds 15 $\mu\text{g/ml}$. Patients suffering hepatotoxic reaction have had jaundice, azotemia, acidosis, hypocalcemia, prolonged prothrombin time, hemorrhagic diathesis including gastrointestinal bleeding, hypotension, and coma; autopsy may reveal extensive fatty changes in the liver.

Jaundice has occurred after use of erythromycin estolate (Ilosone). Robinson¹⁸ noted that in his series of patients receiving the estolate salt, 3.3% became jaundiced. Hepatotoxicity generally reflects one or two weeks of continuous therapy or several courses of the drug. The jaundice, usually a manifestation of intrahepatic cholestasis, subsides rapidly when use of the drug is stopped but reappears promptly if the drug is readministered, usually within 48 hours. Erythromycin, which is not hepatotoxic in its basic form, probably acquires this capacity by esterification of a side chain, that is, when a simple hydroxyl group is replaced by the propionyl radical.

Alterations in hepatic function have occurred in some patients after two weeks or more of therapy with triacetyloleandomycin (Cyclamycin, TAO) in a daily dose of 1 Gm.¹⁸ The abnormal reactions subside after use of the drug is discontinued.

In patients receiving novobiocin, scleral discoloration more often reflects the transient deposition of a harmless pigment produced by the metabolism of novobiocin, rather than hyperbilirubinemia.¹⁹ The yellow pigment has been found in the plasma of patients receiving the drug, and its presence may interfere with determinations of serum bilirubin and the icteric index. In young children, however, novobiocin may interfere with the conjugation of bilirubin and has caused hyperbilirubinemia. When scleral discoloration appears during therapy, administration of the drug should be discontinued until the nature of the pigment can be ascertained. Pigmentation

resulting from the metabolite of novobiocin, as distinguished from that of true jaundice, does not contraindicate continued use of the drug. Because of the possibility of novobiocin-induced hyperbilirubinemia, administration of novobiocin to newborn and young infants should be avoided.

Abnormal results of liver function have occurred in patients receiving lincomycin, but whether jaundice has resulted solely as a consequence of administration of the drug is uncertain.

The sulfonamides appear to have been hepatotoxic, and in the newborn, these drugs may actively compete with bilirubin for protein binding. A substance competing with bilirubin for binding may release the pigment, and this mechanism may be utilized in cases of sulfonamide-induced kernicterus.

Amphotericin B has precipitated acute hepatic failure. On rare occasions, nitrofurantoin and nalidixic acid appear to be hepatotoxic. Whether colistin is hepatotoxic remains uncertain.

Certain drugs including oxacillin, cloxacillin, ampicillin, cephalothin, and nalidixic acid may cause increased serum glutamic oxaloacetic transaminase activity, but it is the consensus that as an isolated finding, this does not necessarily reflect hepatotoxicity.

Administration of chloramphenicol to infants should be discontinued promptly if anorexia, abdominal distention, lethargy, and hypothermia develop. This "gray syndrome," which was alluded to previously, appears to reflect excessive concentration of chloramphenicol in the blood and is the basis for recommending that the drug be given to infants only in those rare instances when its use is imperative. A low level of glucuronyl transferase enzyme activity in the livers of newborn infants has been demonstrated. This enzyme, which is responsible for glucuronide conjugation of bilirubin, increases to normal levels of activity in the first two to three weeks of life. The glucuronide-conjugating mechanism appears necessary for the detoxification of chloramphenicol, and when the enzyme system is immature, it is hypothesized that the "gray syndrome" results.

(Part II Continued Next Month)

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References may be secured from the author or the reprints.

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Examination

You must look into people as well as at them.—Lord Chesterfield

Business is business.

Says who?

Says too many people.

You've probably heard it yourself many times.
It's used to justify almost *anything*.

But how many times have you ever questioned this attitude or raised your voice in protest? An idea like this takes root just because not enough people do anything to stop it.

If you have ever asked yourself "Why doesn't someone do something about it?" you're talking to the right person. You.

It won't be easy. Sometimes you'll need encouragement. The kind you'll find in your place of worship.

Here you'll discover you're not alone. That, in itself, can give you the strength to say "Says who?" once in a while when it needs to be said.



Religion in American Life

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Grand Rounds

Thyrotoxic Heart Disease*

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History

In 1931-1932 Lahey called attention to a clinical variety of hyperthyroidism characterized by apathy rather than hyperactivity, to which he gave the name "apathetic thyroidism."^{1,2,3} Few cases of this entity are described in the literature, but textbooks either fail to mention "apathetic thyroidism" or dismiss it briefly.⁴

In 1930 Hamburger and Lev described thyroid toxicity which was "masked": " - - - men and women at or near the middle decade of life—individuals without exophthalmos, struma or tachycardia, apathetic, listless, with masked facies, dulled eyes, quiet and insensitive, in striking contrast to the alert, restless, nervous, bright, prominent-eyed patient with 'typical' hyperthyroidism."⁵

In discussing the atypical form of hyperthyroidism and its manifestations, it is of interest to trace the history of the description of this disorder. We have touched on the first descriptions of the "masked" form with which we are primarily concerned; but we will also discuss the more common form of hyperthyroidism and related cardiac dysfunction.

Caleb Parry in 1786 described the association of heart disease and enlargement of the thyroid gland.^{6,7,8} In the latter half of the 1830s, Graves and Basedow both described the association of cardiovascular symptoms and exophthalmic goiter.⁶

Trousseau in 1863, by his error of giving tincture of iodine instead of tincture of digitalis to a patient suffering from cardiac failure, established in retrospect the true cause-and-effect relationship of hyperthyroidism on cardiac function.⁶ He stopped the iodine upon discovering the error; nevertheless, the cardiac failure worsened. The clinical importance of iodine was not recognized for another sixty years.⁶

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, Minneapolis, October 4, 1966.

Continued

In 1923 Hamilton, in a review, showed that partial or complete relief of symptoms could be achieved in a large number of patients by thyroidectomy.⁹

Clinical Description

Masked hyperthyroidism is that form of thyroid disease in which the overactive thyroid gland does not produce classic symptoms, but manifests itself by symptoms restricted to a single system.¹⁰ The mono-symptomatic form is described in which disturbances of one system are prominent and suggest disease of that system.⁴ In the older age group the most common form of masked hyperthyroidism presents as cardiovascular disease, either atrial fibrillation, angina pectoris, or congestive heart failure. Of these, the most common is atrial fibrillation.¹⁰

Cases are described where some or most of the so-called classic features of hyperthyroidism are absent.⁴ An important group are those cases where the thyrotoxic signs are not truly atypical but are overshadowed by prominent signs of some other coincidental disease or symptom complex.⁴

Apathy represents a specific, though rather uncommon, response to the hyperthyroid state.⁴ Clinical manifestations include lethargy, placid facies, depressed mood, mental and physical inertia and thus, in general, the opposite of the usual hyperkinetic state.¹¹ Although not limited to the following groups, apathy usually is seen more frequently in the elderly, in patients without goiters or with small nodular goiters, and in patients with prominent cardiovascular symptoms.⁴

Incidence

A large series of 200 thyrotoxic patients revealed 30 per cent as having some cardiac abnormality.¹² This study indicated age to be the main factor in the production of the cardiac disease. The older patients were also found to have a greater incidence of nodular goiter and gave a history of longer duration of symptoms. In 14 per cent of their cases, thyrotoxicosis appeared to be the only cause of the heart disease. The prognosis with regard to mortality, morbidity, and reversion of atrial fibrillation to sinus rhythm was good in this group. The worst prognostic group included those with associated ischemic heart disease. Sandler and Wilson in a study and review of the nature and prognosis of heart disease in thyrotoxicosis show somewhat similar findings in a larger group of patients.¹³

Table 1 presents the analysis of 462 patients with thyrotoxicosis. Forty-three per cent are included in Group III, in which hyperthyroidism was the only known cause of the heart disease.

The progressive increase in incidence of heart disease in thyrotoxicosis with advancing age is well documented.^{12,13} The age distribution was similar in patients with and without associated heart disease.¹³ The female:male ratio in patients with cardiac involvement was 3.4:1; and 4.0:1 in the whole group was close to that in the thyrotoxic patients without cardiac complications.¹³

The incidence of nodular goiter did not appear to be related to the development of cardiac complications.

The incidence of atrial fibrillation and congestive heart failure increased with age, with atrial fibrillation the most important factor in producing congestive heart failure. The prognosis of patients with congestive heart failure is shown in Table 2.¹³ The severity and duration of the thyrotoxic state was not felt to be significant in producing cardiac complications.^{13,14}

Pathology

Schlesinger and Benchimol reported the pathology in four cases of thyrotoxic heart disease in which cardiac involvement was attributed solely to hyperthyroidism in the absence of any other etiologic factor.¹⁵ The rarity of the disorder does not allow for extensive discussion of pathologic findings. Of the author's four cases, three manifested cardiac failure. One patient with heart failure revealed dissociation of myocardial fibers and interstitial edema at autopsy. Cardiac hypertrophy, primarily left ventricular, was found in the fourth patient who had remained compensated prior to death. Changes of serous myocarditis have been described in cases with the pure form of thyrotoxic heart disease.¹⁴

The importance of recognition of the thyrotoxic patient with cardiac dysfunction is that the pure form will respond to appropriate medication. The more chronic and less responsive patients are those in whom underlying organic heart disease already exists. In the latter case, the hemodynamic changes affect a previously damaged heart. Schlesinger and Benchimol feel that heart failure in the pure form is due solely to effects of thyroid hormone on the heart muscle.¹⁴

TABLE 1*

Thyrotoxic patients treated with I 131, January, 1949 to October, 1956		462
Group I. Patients without cardiac involvement		312
Patients with cardiac involvement		150
Group II. With associated organic heart disease		86 (57%)
Ischemic heart disease		43
Hypertensive heart disease		22
Rheumatic heart disease		11
Pulmonary heart disease		8
Congenital heart disease		2
Group III. No evidence of associated heart disease		64 (43%)
Auricular fibrillation		48
Congestive cardiac failure		26
a. With auricular fibrillation		23
b. With sinus rhythm		3
Cardiomegaly alone		13

*From Sandler, G., G. M. Wilson, Quart. J. Med., 28:347, 1959.

TABLE 2*

Prognosis of Congestive Cardiac Failure in 56 Thyrotoxic Patients Following One to Seven Years after I 131 Therapy		
	Group II	Group III
	with	without
	associated	associated
	heart disease	heart disease
	(30 patients)	(26 patients)
Death from congestive failure	23.3%	19.2%
Further attacks of failure while on mersalyl	16.7%	15.4%
No further attacks of failure while on mersalyl and/or digitalis	20.0%	23.1%
Relief of failure with treatment of thyrotoxicosis alone	40.0%	42.3%

*From Sandler, G., G. M. Wilson, Quart. J. Med., 28:347, 1959.

Continued

Goodpasture in 1921 reported two cases of thyrotoxicosis associated with heart failure.¹⁶ He emphasized the pathologic findings of myocardial degeneration, infiltration, necrosis and fibrosis which were considered as specific effects of the thyroid hormone. He also obtained similar changes experimentally.¹⁷

Goodall and Rogers in 1927 and Lewis in 1932 observed a similar type of myocardial lesion in fatal cases of hyperthyroidism and concluded it was due to the direct influence of thyroid secretion on heart muscle.^{18,19}

In 1941 Duchosal and Henny reported the case of a thyrotoxic patient with angina pectoris who died suddenly following thyroidectomy.²⁰ At post-mortem examination the myocardium showed degeneration with areas of interstitial fibrosis but no coronary artery pathology.

In 1948 Lemos Torres described two patients who died from thyrotoxic crises. Autopsy revealed cardiac changes characterized by serous myocarditis with fibroblastic degeneration.¹⁴

Physiology

The physiologic alterations in the thyrotoxic state should help to explain the cardiovascular changes. Although the exact cause of myocardial hypertrophy is not known, it is obvious that circulatory states associated with increased cardiac output and/or vascular resistance result in myocardial hypertrophy. The cause of hypertrophy of the myocardium appears to be related to an increase in the mechanical work of the heart.²¹

Some of the circulatory changes in thyrotoxicosis are increased mean blood pressure in both the pulmonary and systemic circuits, an increased cardiac output and velocity of flow, and an increased pulse rate which is even beyond the increased metabolic requirements of the thyrotoxic state.^{22,23,24}

The findings of left-sided cardiac enlargement can then be explained on the basis of increased mean systemic blood pressure and increased cardiac output. The right-sided changes are not only influenced by the mean pulmonic pressure and cardiac output but may be greatly affected by flow rate.²¹

Cardiac catheterization studies demonstrate an increase in oxygen consumption, cardiac rate, cardiac output, left ventricular work, coronary blood flow, and cardiac oxygen utilization in patients with thyrotoxicosis.²⁵ After treatment, these authors found a decrease in these functions, while coronary vascular resistance increased. These findings are compatible with the works of others in that the coronary vascular response and myocardial metabolic changes are similar to those seen in other tissues in the presence of excessive thyroid hormone.²⁵

A direct alteration of myocardial function by thyroxin has been demonstrated in both clinical and experimental hyperthyroidism.²⁵ The failure of adequate cardiac output response to exercise has been thought to be due to altered enzyme function resulting in impaired myocardial energy production.²⁶ The action of thyroxin on myocardial function may well be mediated by sensitization of the myocardium to sympathetic nerve stimulation and to sympathomimetic amines.²⁷ An increased concentration of catecholamines has been demonstrated in the myocardium of thyrotoxic dogs.²⁸

A dose-response study of euthyroid* and hyperthyroid subjects to intravenous epinephrine demonstrated a greater reactivity of the thyrotoxic group. Differences in the magnitude of increases of oxygen consumption, blood pressure, and heart rate clearly separate the two groups.²⁹ The increased sensitivity to epinephrine was shown not to be due to hypermetabolism. Patients with diseases associated with increased metabolism but normal thyroid function react to epinephrine

*See Test Your Word Score Page 1359.

normally.²⁹ The level of circulating thyroid hormone is felt to be a major factor in determining the response to epinephrine administration.²⁹

Hyperthyroidism in both man and the experimental animal produces an increased susceptibility to cardiac arrhythmia after parenteral administration of epinephrine.³⁰ The frequent occurrence of atrial fibrillation in patients with thyrotoxicosis in the absence of organic heart disease has already been shown. Although atrial fibrillation does not compromise the circulation at rest, impaired circulatory responses to the increased demands of exercise are well documented.³¹ Since the circulation of the hyperthyroid patient is under a constantly increased load even at rest, the importance of this arrhythmia as a factor in the development of congestive failure is evident.³²

In addition to the direct alteration of myocardial function by excess thyroxin, the presence of an increased peripheral circulatory load in these patients is suggested by the occurrence of heart failure at absolute levels of cardiac output which were normal or high.³³ The hemodynamic data in these patients closely resembled in many important respects that obtained in patients with systemic arteriovenous fistulae.³³ The peripheral circulatory load in thyrotoxicosis is hemodynamically similar to that of systemic arteriovenous fistulae. An increase in blood volume is seen in both groups.³³ The continued development of hypervolemia, which initially represents a desirable circulatory adjustment, may well be a factor in the development of myocardial dysfunction because of an increased venous return, overdistention of the heart, and perhaps ultimately the development of atrial fibrillation.³⁴

The development of congestive heart failure may thus occur in thyrotoxicosis for a number of reasons. With inadequate myocardial function resulting from a direct effect of thyroxin on the heart in the presence of sympathomimetic amines and an associated increased circulatory load, the heart with pre-existing organic disease or even the normal heart may fail.³³

The similarities between the cardiovascular effects of excess thyroid hormone and epinephrine administration have stimulated an evaluation of the therapeutic effects of sympathetic blockade in hyperthyroidism. Spinal anesthesia has been shown to prevent hyperkinetic cardiovascular responses during thyroid surgery.³⁵ Drugs which inhibit sympathetic adrenergic functions are thus used clinically in thyrotoxicosis. Guanethidine is a potent adrenergic blocking agent which selectively blocks the reflex responses to sympathetic stimulation, inhibits the uptake of circulatory norepinephrine, enhances the action of injected catecholamines, releases norepinephrine from bound tissue stores, and causes a slow but continuous release of norepinephrine.³⁶ The mechanism responsible for the guanethidine response in thyrotoxicosis may be: Blockage of the effect of tonic sympathetic discharge on the heart; reduction in myocardial catechol content, or reduction of myocardial response to circulating catecholamines.³⁶ The authors demonstrated that parenteral administration of guanethidine returned the elevated heart rate, blood pressure, cardiac output and cardiac work towards normal.³⁶

Clinical Findings

Atrial Fibrillation

All patients with atrial fibrillation, particularly if they do not respond to orthodox therapy, should be suspected of hyperthyroidism. This is true even when a definite cardiac etiology is established. Hyperthyroidism has been reported as the etiologic agent in 3.5 to 14 percent of all cases of atrial fibrillation.¹⁰ Atrial fibrillation occurs in up to 90 percent of hyperthyroid patients.^{14,32,37} Atrial fibrillation in hyper-

Continued

thyroidism increases in incidence with age.

Ernstene reported 1,000 consecutive cases of thyrotoxicosis in which atrial fibrillation occurred in 207.³⁸ Seventy-five percent occurred in patients over the age of 45, although only 25 percent of the 1,000 cases were over this age. Approximately 150 of the 250 patients over the age of 45 fibrillated, an incidence of roughly 60 percent.

The implications of these studies are quite clear. All patients with atrial fibrillation should be studied to rule out thyrotoxicosis.

The reversibility of atrial fibrillation to normal sinus rhythm in patients with hyperthyroidism is of diagnostic, prognostic and therapeutic significance. In most instances in which hyperthyroidism is the only cause of atrial fibrillation, spontaneous reversion to normal sinus rhythm will often occur upon restoration of euthyroidism.³⁹

Angina Pectoris

Those cases with angina associated with thyrotoxicosis in which the precordial pain is not responsive to rest and vasodilator drugs, but which responds to anti-thyroid drugs are of interest. It is postulated the anginal syndrome results from myocardial anoxia due to the direct effects of thyroxin on the heart muscle.¹⁴

Laboratory Diagnosis

The diagnosis of masked hyperthyroidism must largely depend on laboratory methods since absence of classic clinical symptoms is characteristic of this condition.¹⁰

Basal metabolic rate determinations may not be accurate.¹⁰ Congestive heart failure, hypertension, orthopnea, pulmonary disease, and arteriovenous aneurysms may produce elevation of the test. Peripheral edema may in some cases reduce the value of the metabolic rate.

The circulation time is frequently increased in thyrotoxicosis; however, this is not always the case if heart failure exists. Increased circulation time is suggestive of hyperthyroidism if anemia, fever and vitamin B deficiencies have been excluded.¹⁰

The serum protein-bound iodine has been reported to be decreased, and thus in error, if patients have received mercurial diuretics.³⁹

Radioactive iodine uptake is not affected by non-thyroid cardiac disease or by any other extrathyroid factor which may affect other tests, except for certain medications.¹⁰

Radiologic aids are often important and helpful. Generalized cardiac enlargement may be a common radiologic finding in thyrotoxicosis and may be preceded by enlargement of the pulmonary artery.¹³ Prominence of the main pulmonary artery alone or in combination with a high or prominent aortic arch has been noted.²¹ Cardiac enlargement in the absence of congestive failure was unusual. When cardiac enlargement was present, the left ventricle was the predominant chamber.^{15,21,22} The roentgenographically abnormal patients showed a greater pulse rate and mean blood pressure than other patients with thyrotoxicosis.²¹

When electrocardiographic evidence of left ventricular hypertrophy exists with no radiologic evidence of enlargement, a return of the electrocardiogram to normal may occur after treatment.¹³ The presence of both radiologic and electrocardiographic changes represents a more severe and permanent form of cardiac damage which may not be reversible.¹³

Treatment

In patients with thyrotoxicosis it is often difficult to assess accurately or objectively the response to digitalis. As reported in a sizeable series of patients with congestive heart failure and/or atrial fibrillation associated with hyperthyroidism the therapeutic response was quite definite even before the euthyroid state was established.³⁹ The usual degree of slowing of the ventricular rate after digitalis administration is not noted in these patients. The dosage of digitalis is increased significantly in patients with hyperthyroidism.³⁹ Digitalis is clearly indicated and is beneficial in congestive heart failure accompanying hyperthyroidism. Ultimate correction of the metabolic burden of hyperthyroidism on the heart and circulation will, however, not be accomplished until the thyroid disorder is successfully controlled.³⁹

We have previously discussed the use of agents such as guanethidine. This drug is recommended in severe overt hyperthyroidism because of its potent and unique sympatholytic effects, thus ameliorating promptly and effectively those signs and symptoms of thyrotoxicosis due to sympathetic hyperactivity without affecting the function of the thyroid gland.⁴⁰ The dosage of guanethidine is usually 50 to 100 mgm. initially.⁴⁰ A single oral daily dose or divided doses orally or intramuscularly is recommended. Twenty-five mgm. increments every third day are given until a therapeutic end-point is reached. One observes complete control of signs and symptoms of the disease or distinct orthostatic hypotension. The dose at which an end-point is reached is then continued as maintenance. In Waldstein's series, a satisfactory response was achieved on the average by six days and not later than the second week of therapy.⁴⁰ Thus, like digitalis in some respects, guanethidine does not correct the basic hormonal disturbance; it can only be considered an adjunct to definitive therapy and recommended for short-term aid in the management of the thyrotoxic patient with severe heart failure.^{36,40}

The importance and need for agents such as propylthiouracil and methimazole are well known and require little explanation.

Thyroidectomy today in patients with heart disease is not the disastrous ordeal it was prior to the development of antithyroid medication. Goitrogenic therapy allows for subtotal thyroidectomy in selected patients. However, radioactive iodine in adequate doses is rapidly replacing surgical thyroidectomy because of its simplicity of administration, predictable effectiveness, paucity of complications and obviation of the need for hospitalization.³⁹

In one series, approximately one third of patients with atrial fibrillation reverted spontaneously to normal rhythm after radioactive iodine.¹³ More than one half of the patients with congestive failure had no further attacks of failure after radioactive iodine, and more than one third required no further treatment with digitalis.

The prognosis was adversely affected when atrial fibrillation was associated with congestive heart failure.¹³ The rate of reversion with radioactive iodine was higher in younger patients. The over-all prognosis was more favorable if sinus rhythm could be restored in patients with congestive heart failure and atrial fibrillation. Radioactive iodine therapy is safe and effective and is the treatment of choice in thyrotoxic patients with severe cardiac complications.¹³

Case Report

A 56-year-old white, widowed, female cleaning woman, was admitted for the first time to Hennepin County General Hospital on 7/12/66.

Two weeks prior to admission the patient noted the onset of progressive pedal edema which progressed to the sacral region. Accompanying the edema was dyspnea on exertion progressing to orthopnea and paroxysmal nocturnal dyspnea. The patient complained of palpitations. Also

Continued

noted were occasional bouts of low substernal chest pain.

The patient was seen by a private physician, who made a diagnosis of congestive heart failure, administered 2 cc. of thiomerin parenterally, and referred the patient for admission to this hospital.

Physical examination on admission revealed a woman appearing older than her stated age with apathetic facies, flattened affect, suggestion of a stare, and in moderate respiratory distress.

The blood pressure was 130/80, respirations 28, regular but labored, and the apical pulse irregular and approximately 150.

Marked distention of the neck veins with filling from below was noted. Examination of the chest revealed bilateral dullness at the bases with medium to coarse, moist rales. The left cardiac border was found to be in the mid-clavicular line, fifth intercostal space. A protodiastolic gallop was present. No murmurs were audible. A_2 equal to P_2 .

The liver was enlarged three fingerbreadths below the right subcostal margin and was tender. Questionable ascites was present. Pitting edema was present from the abdominal wall inferiorly to the feet bilaterally. No neurologic abnormality was noted. No tremor was present. The reflexes were only slightly hyperactive and equal.

Chest x-ray revealed bilateral pleural effusions with slight cardiac enlargement. Electrocardiograms revealed atrial fibrillation and right axis deviation.

Hemoglobin was 12.4 grams percent. Cholesterol was 150 mg. percent. Normal liver and renal function studies were obtained.

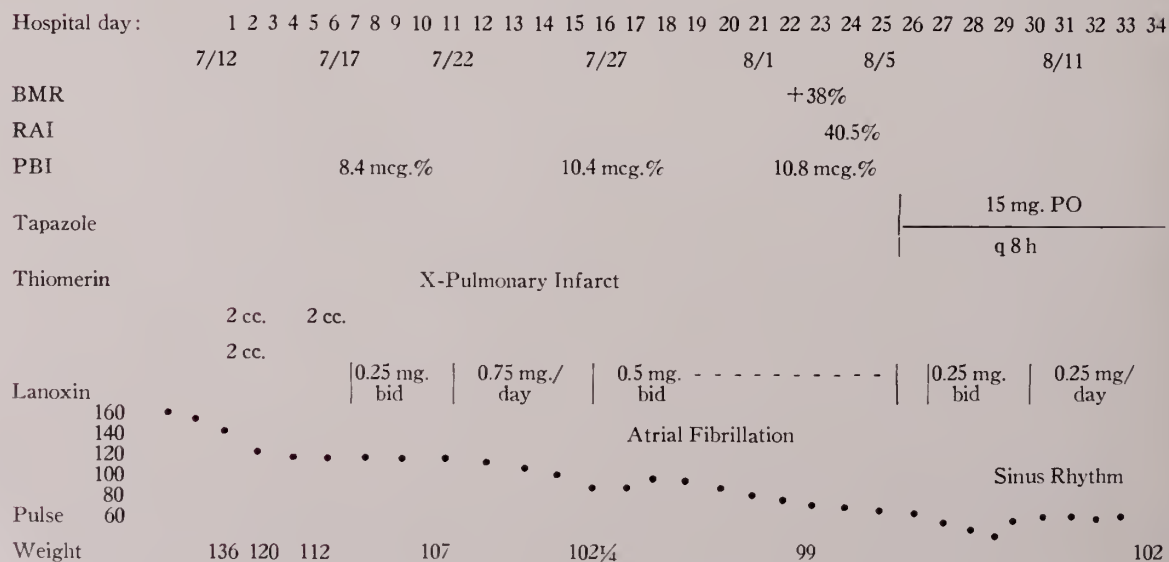
Hospital course (Figure 1): The patient was given 2 cc. of thiomerin parenterally on 7/12/66 and 7/14/66. A dose of Lanoxin of 3.0 mg. was administered orally over the next 24 hours. Maintenance of 0.25 mg. Lanoxin twice a day was increased on 7/18/66 to 0.5 mg. in the A.M. and 0.25 mg. in the afternoon orally. On 7/22/66 the dosage of Lanoxin was increased to 0.5 mg. orally twice a day through 8/5/66. The pulse rate did not fall below the range of 100 to 110 until the latter dose was started.

A diuresis of 16 pounds occurred within 48 hours and 24 pounds by the end of five days. A total loss of 37 pounds had occurred by the 23rd day.

On the 10th hospital day, the patient experienced sharp right-sided pleuritic chest pain. Clinical, radiological and laboratory studies confirmed the presence of a pulmonary infarct. The patient was treated with heparin with an excellent response.

A serum protein-bound iodine (PBI) drawn on 7/17/66 was 8.4 mcg. percent. A second PBI drawn on 7/26/66 was later reported as 10.4 mcg. percent. A third PBI drawn on 8/2/66 was 10.8 mcg. percent. On 8/4/66 a radioactive iodine uptake was performed and was 40.5 percent at 24 hours. However, the patient had an emesis shortly after receiving her iodine

Figure 1



dose and thus the uptake may have been inaccurate. A basal metabolic rate determination was +38 percent on 8/3/66.

Tapazole was begun on 8/6/66, at a dosage of 15 mg. orally every eight hours. Within 24 hours the dose of Lanoxin was halved because of the ventricular response and in five days only 0.25 mg. per day was required. On the sixth day of Tapazole, the patient's cardiac arrhythmia converted to a normal sinus rhythm. She had noticed marked symptomatic improvement in terms of mood elevation, less fatigue, increasing appetite and weight gain.

The patient was discharged three days after conversion to sinus rhythm and was seen in the Outpatient Department two weeks later. She had gained eight pounds and felt better than she had in some time. Lanoxin was discontinued and Tapazole was tapered over a three-month period.

The thyroid I¹³¹ uptake was repeated after stopping Tapazole for 10 days, three months after discharge from the hospital, and was 67 per cent at 24 hours. The patient was then treated with radioactive iodine.

References

1. Lahey, F. H.: Ann Surg 93:1026, 1931.
2. Lahey, F. H.: New Engl J Med 204:747, 1931.
3. Lahey, F. H.: Ann Intern Med 5:1123, 1932.
4. McGee, R. R., et al.: Ann Intern Med 50:1418, 1959.
5. Hamburger, W. W., M. W. Lev: JAMA 94:2050, 1930.
6. Ginsburg, A. M.: Ann Intern Med 5:505, 1931.
7. Phillips, J., J. P. Anderson: JAMA 89:1380, 1927.
8. Parry, C. H.: Collections from the Unpublished Medical Writings of the Late Caleb Hillier Parry, Vol. II, London, Underwoods Fleet Street, 1825.
9. Hamilton, B. E.: JAMA 80:1771, 1923.
10. Bortin, M. M., et al.: Amer J Med 11:40, 1951.
11. Hare, L. J., J. O. Ritchey: Ann Intern Med 24:634, 1946.
12. Summers, V. K., S. J. Surtees: Acta Med Scand 169:661, 1961.
13. Sandler, G., G. M. Wilson: Quart J Med 28:347, 1959.
14. Griswold, D., J. H. Keating, Jr.: Amer Heart J 38:813, 1949.
15. Schlesinger, P., A. B. Benchimol.: Amer J Cardiol 2:430, 1958.
- 16-40. May be secured from the author or the reprints.

Quick Work

Sodbuster doctors operated on threshers' mangled legs on a parlor sofa, the kitchen table, or the familiar door placed on saw-horses. They set fractured femurs with a piece of string and a flatiron. They executed podalic versions on the kitchen table. They still were men who brooked no delay. When Dr. William Mayo visited a Minnesota granger farm, he spoke to a small boy. The child replied with a twisted tongue.

"Why, that child is tongue-tied," exclaimed the doctor. "Come here, George!"

The boy climbed on his knee as Dr. Mayo took out a pair of scissors from his pocket case. The lad opened his mouth; the doctor snipped the membrane that bound his tongue. He gave the youngster an affectionate pat and sent him on his way. The boy used his untied tongue so well he grew up to be a judge.*

*Richard Dunlop, M.D.: Doctors of the American Frontier.

Health

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—Josh Billings



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so smoothly that patients are often untroubled
by either disease *or* therapy**

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in mild to moderate cases, often effective at half the usual thiazide or thiazide/reserpine dosage.

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controls many moderate to severe cases without any need for ganglionic blockers, or other more potent agents; if such agents are needed, their dosage can be cut in half.

BUTISOL® (butabarbital) 30 mg. (½ gr.)†;
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*15 mg. of Butisol (butabarbital), plus the other ingredients, in outer layer; 15 mg. of Butisol (butabarbital) in a specially coated core for delayed action, to approximately equalize duration of action for all components.

Contraindicated in presence of renal impairment, peptic ulcer, ulcerative colitis, or mental depression, and in patients with porphyria or those sensitive to any component. **Warning:** Coated potassium tablets, sometimes administered in conjunction with anti-hypertensive therapy, may be associated with small bowel lesions which have led to obstruction hemorrhage, and perforation. Surgery has been required and deaths have occurred. Such tablets should be used only when indicated and when adequate dietary supplementation is not practical. They should be discontinued immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occur. **Precautions:** Exercise caution in hepatic disease, diabetes, surgery, coronary artery disease, epilepsy, E.S.T., and in patients receiving digitalis. **Side Effects:** Electrolyte imbalance, hyponatremia, hypochloremic alkalosis and/or hypokalemia, hyper-

uricemia and gout, bradycardia, drowsiness, skin rashes, hangover, systemic disturbances, weakness, leg cramps, diarrhea, epistaxis, dizziness, urticaria, dry itching skin, nausea, vomiting, palpitation, superficial skin bruises, headache, dehydration, paresthesias, photosensitivity, pancreatitis, jaundice, xanthopsia, thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, nasal congestion, hypotension, lassitude, loose stools, anorexia, bizarre dreams, peptic ulcer, ulcerative colitis, mental depression. (Ammonium chloride, which may be administered to reverse hypochloremic alkalosis, should not be given to patients with hepatic disease.) **Before prescribing or administering, see package insert.** †Warning: May be habit forming. **Usual Adult Dosage:** Butiserpazide®-25 or Butiserpazide®-50: 1 tablet daily or b.i.d. **References:** 1. Johnson, H. J., Jr.: *Penna. M. J.*: 67:35, 1964. 2. Coodley, E. L.: *Curr. Ther. Res.* 4:460, 1962.

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WANTED: GP to join clinic serving population area of 12,000. City has new hospital, new clinic building, two nursing homes, new Jr-Sr high school, new swimming pool, rich farming area in Red River Valley. Fishing and hunting nearby; metropolitan city close by. Salary open and partnership if interested. Write or call Warren Clinic, Warren, Minnesota 742-6231, area code 218.

GENERAL PRACTICE associate wanted for young three man group in populous growing area located 30 minutes south of the Twin Cities. Spacious three year old clinic with new accredited hospital and nursing home in same town. Salary and terms open. Contact River's Edge Medical Clinic, Farmington, Minnesota. Telephone 463-7181.

WANTED: General practitioner, to join two G.P.'s well established in north central Minnesota community, 2200 pop., 65 miles from Twin Cities. Excellent office space with lab and X-ray, just opened new hospital, all facilities. Assistantship or partnership. Considerable surgery and obstetrics. Hunting, fishing, golf club. Great opening for interested G.P. WRITE MINNESOTA MEDICINE—381; 375 Jackson, St. Paul, 55101.

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Continued

GENERAL PRACTITIONER wanted to join well-established practitioner. New clinic building—90 miles east of St. Paul—city of 14,000. Early partnership with full hospital facilities. Ideal location. L. W. Picotte, M.D.; Chippewa Falls, Wisconsin.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X-ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE—289; 375 Jackson, St. Paul, 55101.

BEAUTIFUL NEW OFFICE available now for second office or solo practice. Wonderful opportunity, progressive area, only specialists in area now are OB/Gyn. Excellent lease arrangement. Look into this. Write: MINNESOTA MEDICINE—375; 375 Jackson, St. Paul, 55101.

GENERAL PRACTITIONERS AND INTERNISTS to join eight-man group in fascinating San Francisco. Locum tenens also available. Will meet reasonable salary request. A. J. Franzi, M.D., 3620 Army St., San Francisco, Calif. 94110.

IDEAL SPACE AVAILABLE. New modern building, ideal location Como Avenue, St. Paul University Campus. Will partition to your specifications. Call 644-5742 or 646-3933, St. Paul.

GENERAL PRACTITIONER wanted to join three man general practice group situated in a new clinic building in Stillwater, Minnesota (Community of 10,000), new hospital in town. Also need locum tenens immediately. Call 439-2215 up to 6:00 p.m. or 439-3020 after 6:00 p.m.

WANTED GENERAL PRACTITIONER, General Surgeon, Obstetrician for active group clinic in Minneapolis suburb. Now six man group including full time surgeon and obstetrician. New clinic facilities and two new hospitals near by. Salary open. Partnership offered after short trial period. Coon Rapids Clinic, 9920 Zilla Street, N.W., Coon Rapids, Minn. 55433.

WANTED: GENERAL SURGEON to fill vacancy with well established eight man group. Beautiful award winning clinic just blocks from new 120 bed hospital. Picturesque community of 15,000 located on the Mississippi River with good recreational facilities, schools and churches. An excellent opportunity in a growing environment. Salary one year, then partnership. Write: Harry Williams, M.D., Medical Block Clinic, Red Wing, Minnesota, or call 507, 388-4751.

GENERAL PRACTITIONER desires position with group or partnership in town of 3000 population or more, preferably within 100 miles radius of Twin Cities. Currently in solo practice including surgery and OB at same location for 12 years. Write: MINNESOTA MEDICINE—383, 375 Jackson, St. Paul, 55101.

WANTED: Young, energetic General Practitioner to join one man clinic. Salary open. Contact: Maurice Meller, M.D., Brainerd Clinic, Brainerd, Minnesota.

INTERNIST, PEDIATRICIAN and OB-gynecologist wanted to join two general surgeons in a rapidly grow-

ing practice. Attractive town of 3,000 on large lake 30 miles west of Twin Cities. New 55-bed JCAH hospital with plans for major expansion. Five other physicians in town. No OB-GYN, internist or pediatrician in area. Medical community serves in an area with population of 20,000 to 25,000. Planning to expand into partnership multi-specialty clinic. Call or write: Savaryn Clinic, Waconia, Minnesota 55387. Telephone: 442-2137.

GENERAL PRACTICE available North Central Minnesota. Well equipped office. New hospital in town. Good records. Terms could be arranged like rent. Write: MINNESOTA MEDICINE—384, 375 Jackson, St. Paul, 55101.

WANTED: Locum Tenens for general practice for February 1968. Salary open. Contact: Maurice Meller, M.D., Brainerd Clinic, Brainerd, Minnesota.

THREE MAN group in North West Wisconsin Resort, State Conservation and Retirement Area needs two more physicians adequately to serve their practice. Facilities offered are three-room physician suites, X-ray and lab under AMT technician, RN-only nursing personnel. New accredited thirty-two bed hospital and forty-six bed nursing home. Deer and duck hunting, fishing within five minutes of town. Internist most needed; generalists welcomed. Will meet any reasonable salary request. Partnership after one year. Write: MINNESOTA MEDICINE — 365; 375 Jackson, St. Paul 55101.

OPENING IN MT. LAKE, Minnesota for General Practice. Associate practice if desired, adequate vacations, excellent office space, financial help if needed, new 25-bed hospital, nursing home, two old people's homes, over 100-bed capacity in total. Excellent schools and churches. If interested, call collect 427-3515 Mt. Lake, Minnesota or contact Steinle Drug.

WANTED ASSOCIATE for young general practitioner. Excellent clinic and hospital facilities. Salary or partnership. Agricultural and resort area, good hunting and fishing. Write: Lewis E. Struthers, M.D., Parkers Prairie, Minnesota. Telephone: 218-338-4471 (residence) or 218-338-4371 (clinic).

PHYSICIAN WANTED: to manage new emergency room facilities in St. Cloud Hospital, St. Cloud, Minnesota. Salary and working arrangements open. Write: MINNESOTA MEDICINE — 384, 375 Jackson, St. Paul 55101.

EXPERIENCED GENERAL PRACTITIONER available for locum tenens for the month of September and October 1967. Available after September 10th for periods of one or two weeks duration. Write: MINNESOTA MEDICINE — 385, 375 Jackson, St. Paul 55101.

WANTED: G.P. to take over practice located in East Side of St. Paul, including equipment and lease, all available with good financing. Retiring G.P. will practice to acquaint buyer with patients. Write: MINNESOTA MEDICINE—386, 375 Jackson, St. Paul 55101.

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DOCTORS OFFICES—366 North Prior, St. Paul, Minnesota. One story building recently vacated by 4 doctors. Complete facilities. Good condition. For sale or lease with option to buy. Call Mr. St. Onge 222-1721 or 698-5232. Dunn & Stringer—Realtors.

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GENERAL PRACTICE OPENING—to affiliate with two well-established young G.P.'s—substantial young family type practice—rapidly growing suburb of Des Moines, Iowa—beautiful new clinic with excellent facilities, including x-ray, EKG, lab, and PT—excellent starting salary, liberal time off, and early partnership available—contact Urbandale Medical Clinic—6762 Douglas, Des Moines, Iowa 50322

TOP INVESTMENT—1599 Selby Avenue, St. Paul, Minnesota. 5400 sq. ft. Midway location building with full bsmt. Occupied by triple A tenant under 5 yr. lease. Shows excellent return. Sale wanted, call Mr. St. Onge 222-1721 or 698-5232. Dunn & Stringer—Realtors.

Continuation Course in Neurological Emergencies November 8-10, 1967

A continuation course in Neurological Emergencies will be presented by the University of Minnesota from November 8 to 10, 1967, at the Nolte Center for Continuing Education. This course is designed to present material concerning emergencies of the neurological system and the diagnostic and therapeutic methods of managing them. The program is listed below.

The course will be presented under the direction of DOCTORS A. B. BAKER, Professor and Director, Division of Neurology; and ROBERT W. SOLL, Instructor, Division of Neurology.

Wednesday, November 8

Acute Spinal Cord Compression

8:55- 9:00 Introduction Fred E. Berger,
Albert Sullivan, Jr.

Chairman: Robert W. Soll

9:00- 9:45 Traumatic Fracture—Dislocation of Vertebrae Shelley N. Chou

9:45-10:30 Centrally Herniated Discs... Alfred Uihlein

10:45-11:30 Spinal Cord Compression Due to Neoplasm
Donlin M. Long

Infections and Electrolyte Disturbances

Chairman: A. B. Baker

1:30- 2:00 Purulent Meningitis .. Thomas R. H. Johns

2:00- 2:30 Encephalitis and Post Infections Encephalomyelitis Michael E. Blaw

2:30- 3:00 Acute Syndromes Secondary to Major Electrolyte and Water Disturbances John A. Logothetis

3:15- 3:45 Sinus Thrombosis and Brain Abscess.
Zondal R. Miller

3:45- 4:15 Tetanus A. B. Baker

Thursday, November 9

Bulbar Palsy

Chairman: Harold H. Noran

9:00- 9:30 Poliomyelitis Harold H. Noran

9:30-10:00 Pseudobulbar Palsy George C. Flora

10:00-10:30 Myasthenia William R. Kennedy

10:45-11:30 Guillain-Barré Syndrome David Daly

Stupor and Coma

Chairman: Milton Alter

1:30- 2:00 Examination of the Unconscious Patient
Milton Alter

2:00- 2:30 Acute Intoxications. Edward Jimenez-Pabon

2:30- 3:00 Extradural and Subdural Hematoma .. Ross H. Miller

3:15- 4:00 Coma Due to Metabolic and Endocrine Disorders Thomas R. H. Johns

Friday, November 10

Increased Intracranial Pressure and Visual Loss

Chairman: Sidney K. Shapiro

9:00- 9:30 Brain Stem Herniation. William E. Bradley

9:30-10:00 Optic Neuritis James A. Moriarty

10:00-10:30 Rapid Visual Loss Associated with Intracranial Disease Robert J. Goldberg

10:45-11:30 Cerebral Edema and Benign Intracranial Hypertension Anna L. Ellington

Cerebrovascular Disease and Convulsive Disorders

Chairman: Fernando Torres

1:30- 2:00 Acute Completed Strokes Clark H. Millikan

2:00- 2:30 Internal Carotid Insufficiency William J. Riley

2:30- 3:00 Basilar Vertebral Insufficiency Arthur C. Klassen

3:15- 3:45 Grand Mal Seizures Fernando Torres

3:45- 4:15 Status Epilepticus David Daly

Law and Medicine

The Minnesota Hospitalization and Commitment Act

THE ACT closely resembles recent enactments in Alaska, Illinois, Michigan, Ohio, Pennsylvania and Texas, which are likewise designed to render access to treatment facilities easier for persons in need thereof, while maximally preserving civil rights and humane consideration of these persons.

Application

The Act explicitly applies to public and private hospitals and institutions,* unlike its predecessor, which applied only to state hospitals unless otherwise specified.** In the past, private and general hospitals often followed statutory provisions, such as having a patient sign an agreement to give three days notice of departure from the hospital, during which time personnel felt legally justified in holding him against his will. The hospitals and institutions were not protected at all by the statute, plainly inapplicable to such facilities.

Informal Admission Procedure

Section 3 will remove the requirement of present §525.75 that a psychiatric patient voluntarily entering a hospital sign a formal application. This facilitates admission of patients of borderline mentation whose written consent would be of doubtful legality. It also avoids frightening away from needed care individuals whose paranoid attitude makes them suspicious of signing a formal documents.

*Section 2, Subdivision 8.

**Minnesota Statutes Annotated §525.749, Subdivision 8.

†§525.751, Subdivision 2.

Emergency Hospitalization

The present law† providing for emergency detention on a physician's certificate, applies only in state hospitals. Section 4 Subdivision 1 of the new Act will allow admission or detention and emergency treatment of a person whom a licensed physician has examined within the last 15 days and whom he believes to be mentally ill and in imminent danger of causing injury to himself or others if not immediately restrained.

Restates Common Law

Probably in the absence of such a statutory provision detention under these conditions would not sustain a charge of false imprisonment against hospital and physician. Subdivisions 1 and 2 make such a physician's statement sufficient authority for a peace or health officer to transport the person to a hospital. (An officer probably has this authority at common law too.)

Protects Patient

This section is actually a limitation upon the emergency authority of physician and officer: the person may receive care no more extensive than covers the emergency condition; it must be an emergency such that a court order of commitment cannot be obtained in time to prevent injury; the physician's statement must be in writing. These requirements and the precise wording of the section should help to prevent abuse of the power granted.

Continued

Patient Protected from Being Railroaded

A person who becomes a patient by emergency hospitalization is to be discharged within 72 hours unless a petition for commitment has been filed within that time.

Right to Communicate

This is one of many provisions* protecting against the "railroading" of people into a mental hospital, which appears to be widely feared. A further protection lies in Section 5 Subdivision 1, which entitles the emergency patient to communicate with others outside the hospital and in particular entitles him to private consultation with his attorney and his private physician. The right to consult an attorney probably exists in the absence of statute for any person confined against his will. The right to consult a private physician is a creature of statute. Neither provision has its counterpart in existing Minnesota law; both further protect against "railroading."

The right to communicate with physicians and attorney will also be granted by Section 7 Subdivision 4 to those hospitalized on petition for judicial commitment. Additionally, it will be mandatory for the patient to be informed of this right in writing at the time of his admission.

Right To Be Discharged

Further protection against "railroading" is contained in Section 6 Subdivisions 1 and 2 of the new Act: every patient held under emergency hospitalization must be examined not more than 48 hours after admission. He will be entitled to be discharged as of right should the examination not be held or should the examiner fail to certify to the head of the hospital that the patient is mentally ill and in need of care, treatment and evaluation.

Habeas Corpus Assured

A writ of habeas corpus is the traditional challenge to an unlawful detention of the person. The patient's right to immediate discharge will be enforceable by the writ, specifically preserved in Section 21 Subdivision 3 of the new Act.

*Subdivisions 6 through 15 of Section 7 deal with procedural due process: notice, right to counsel, right to be heard and to present witness. The counterparts in the present law are in §525.751 Subdivisions 2 and 4.

Hearing Required Within 30 Days

A person detained by court order upon a petition of commitment must be granted a hearing within 30 days after filing the petition except for good cause shown, according to Section 7 Subdivision 8 of the new Act.

Abuse of Hold Order

§525.751 Subdivision 2 of the present law authorizes the court to order confinement of a person in a hospital or other place for observation and examination. Under this provision a number of people were confined in one state hospital indefinitely, the hospital administration apparently feeling bound to continue to execute the court order indefinitely, a concrete and probably erroneous interpretation of the order. Since the present law, unlike the new Act, does not require informing a patient of his rights, acceptance by these patients of their plight was understandable.

Under the new Act a patient falls under emergency hospitalization with its examination and certification required within 48 hours or falls under judicial commitment with hearing mandatory within 30 days. Since no isolated provision for a hold order exists under the new Act, abuse thereof cannot occur as happened under present law.

Judicial Commitment

In accordance with the new Act a petition initiating commitment proceedings may be filed by any interested person (under Section 7 Subdivision 1). Present law, nearly as broad, allows any relative or reputable resident to file a petition (§525.751 Subdivision 1).

Arbitrary Refusal of Petitions Curbed

Under the present law in Hennepin County the probate court commissioner's office rejected petitions filed by persons other than immediate family members, notwithstanding the broadness of the statutory provision. The new section makes filing of a petition by the probate court mandatory when the requirements of the section are met. This should discourage the arbitrary local practice described above.

Physician's Certificate Required

However, under the new Act, unlike under

present law, the petition must be accompanied by a physician's certificate stating that he has examined the proposed patient and that he believes the latter should be hospitalized or by a statement that such examination could not be obtained or could not be performed. This section is designed further to protect the patient from unnecessary commitment by a determination of need for hospitalization prior thereto.

In Hennepin County the rules of procedure for the probate court commissioner's office presently require before the filing of a petition a written recommendation by a licensed physician that psychiatric examination and evaluation are indicated. The purpose of this requirement is plainly preselection similar to Section 7 Subdivision 1 of the new Act, but the Hennepin County rule improperly obstructs the broad permissiveness of the present law as the legislature drafted it.

Psychologist May Be an Examiner

After filing of the petition, the court shall appoint two designated examiners to assess the patient's mental condition and report their findings to the court*, thereby tending to insure that the patient's mental condition will be assessed by at least one person skilled in psychiatric evaluation.

Humane Innovations

Accompanied by Interested Person

In addition to procedural due process the new sections provide some purely humane innovations. For example, Section 7 Subdivision 6 requires personal service of notice upon the patient to be effected by a person not in uniform. Notice may be omitted if the court believes it would be injurious to him, provided a guardian ad litem is appointed to receive notice for the patient.

Absent From Hearing

Subdivision 12 permits the patient to be absent from the hearing provided the hearing officer shall have observed and consulted with him previously. This provision is to spare the patient from a

traumatic experience. Presumably the decision to absent the patient from the hearing will be made upon the urging of counsel and psychiatrist; it is doubtful that the court will be as capable of distinguishing its own projected or empathic feelings for the patient from recognition that the hearing for many patients may be a corrective emotional experience promoting improved reality testing.

Protection From Drugging

Subdivision 12 requires that the patient not be so drugged or medicated as to be hampered in preparing or participating in the proceedings.

Misguided Administrative Zeal

Already in Hennepin County the probate court commissioner has required discontinuance of medication prior to the hearing except where absolutely necessary to control the patient. Such a requirement represents excessive administrative zeal: withdrawal of tranquilizing medication which is not so heavy as to obtund the patient permits return of psychotic symptoms which the medication often effectively eliminates. The return of the symptoms may be destructive to a patient. Presumably the value of the relapse would be to demonstrate to the court the patient's underlying, untreated condition. However, that is the function of the designated examiners and of the hospital staff who care for and observe the patient prior to the hearing. The language of the new statute is sufficiently clear to end this administrative fiat.

Avoiding a Constitutional Issue

Subdivision 12 also permits exclusion from the hearings of any person not necessary to the conduct of the proceedings. Plainly the laudable object is to spare the patient embarrassment. In that case, exclusion of a spectator should be on the patient's motion, to be consistent with legislative intent and avoid the constitutional question of the patient's right to a public trial.

Confinement in Jail Forbidden

Section 10 Subdivision 1 of the new law will forbid housing a patient who is detained under any provision of the Act in a jail. This will necessitate use of more distant facilities in those parts

Continued

*Section 7 Subdivision 2 is essentially similar in this respect to §§25.752 Subdivisions 1 and 3, but Section 1 Subdivision 6 of the new law will permit appointment of a certified consulting psychologist as one of the designated examiners in those areas of the state where no psychiatrist is available.

of the state not yet endowed with local psychiatric units. It may thus stimulate construction of needed psychiatric facilities locally where none now exist, where the degrading use of a jail cell to house a mental patient is now justified on grounds of expediency.

After Commitment

Release of patients following commitment is covered by Section 15 of the new Act.*

Review Board Created

The review board created by Section 16 Subdivision 1 consists of at least three people, one of whom "shall be qualified in the diagnosis of mental illness or mental deficiency" and one of whom "shall be learned in the law."

Right to Appear Before Board

Every six months the board shall visit each state hospital, at which time the board shall review the admission and retention of patients who request such review and report its findings to the commissioner. The avowed purpose of the section is to provide investigation of cases where there is doubt as to continuing need for confinement. The compensation provided in Subdivision 6, \$30 per day, is grossly inadequate for the services of a lawyer or psychiatrist and is bound to promote only the most cursory performance of the board's statutory duties.

Rights of Patients

Subdivision 1 of Section 17 will sharply restrict the use of restraints.

Subdivision 2 assures the patient's right to correspond without censorship with certain officials and with his physician and attorneys.

Subdivisions 3 and 4 will assure the patient's right to correspond without censorship with a registered individual other than the foregoing.

Subdivisions 5 and 6 will authorize restriction of the patient's communication with outsiders and receiving visitors where necessary for the medical welfare of the patient, although his personal physician and attorney shall be admitted at all reasonable times.

These subdivisions leave the clinician latitude in protecting the patient from his own indiscretions and from conduct which he might later regret. An example is the patient receiving electroshock. He may show transient coprolalia,* sexual aggression or simply incoherence. For this brief period it would be desirable to limit telephone calls and visits to named individuals who understand the situation rather than to allow the patient to humiliate himself unawares. No such rationale justifies cutting him off from physician or attorney. Nor in the example given is loss of civil rights for the entire period of the patient's hospitalization warranted.

Subdivision 8 will require consent of a patient for a serious surgical operation unless he has been previously adjudged legally incompetent.

Civil Rights Preserved

Perhaps the most sweeping reform is effected in Section 18, which provides that

(Subdivision 1): ". . . no person by reason of commitment, hospitalization, or treatment pursuant to this act shall be deprived of any legal right, including but not limited to the right to dispose of property, sue and be sued, execute instruments, make purchases, enter into contractual relationships, vote, and hold a driver's license. Commitment, hospitalization, or treatment of any patient pursuant to this act is not a judicial determination of legal incompetency . . ."

Subdivision 2 clearly establishes that determination of legal incompetency is a separate undertaking, which may be initiated before, during or after commitment proceedings.

A person acquitted as mentally ill under present law loses by statute or by administrative ruling all of the rights and powers preserved in the quoted new statutory provision, since his commitment operates as an adjudication of incompetency.

Mental Illness Does Not Imply Incompetence in Fact

The new Act recognizes that the degree to which mental illness impairs function varies widely and frequently has little to do with the rights which traditionally have been withdrawn from the mentally ill. It is far preferable to restrict pa-

*Substantially restates §525.753 Subdivisions 4, 6 and 7, §525.762 Subdivision 1, §253.18, §525.761 Subdivision 2 and §246.013.

**See Test Your Word Score Page 1359.

tients in particular activities on an individual basis rather than to blight an entire hospital population indiscriminately. For patients who are thought to be incompetent in fact separate statutory machinery will be available to protect them under the new Act.

Protection of the public will be achieved by curtailing the individual patient's activities as with passes or provisional discharge, which can be granted upon suitable conditions.

*New York Bar, the District of Columbia Bar and the Minnesota Bar.

Conclusion

Protecting the patient from his self-destructive conduct while at the same time preserving his constitutional rights to the maximum extent should be the goal of a truly progressive commitment statute. That goal demands psychiatric sophistication together with good legal draftmanship. With minor flaws the Minnesota Hospitalization and Commitment Act meets these demands admirably.

Barlow Smith, LL.B., M.D.*
Minneapolis, Minnesota

Southern Minnesota Medical Association Meeting

September 15, Faribault

The program for the meeting is listed below:

Carotid Endarterectomy in a Community Hospital—Case Report

J. G. Beaton, M.D.—Northfield
R. H. Meyer, M.D.—Faribault

Experimental Study on Complete Heart Block

D. W. Hannon, M.D.—St. Paul

The Ruptured Abdominal Aneurysm—A Diagnostic Problem

W. R. Schmidt, M.D.—Minneapolis

The Treatment of Acute and Chronic Sinusitis

C. F. Lake, M.D.—Rochester

Predictabilities of Back Injuries from the Orthopedic Surgeon's Standpoint

L. F. A. Peterson, M.D.—Rochester

Chemotherapy in Advanced Cancer

Moderator: Harry F. Bisel, M.D.—Rochester
Breast: John H. Brown, M.D.—St. Louis Park
G. I. Malignancy: Charles G. Moertel, M.D.—Rochester
Pulmonary Carcinoma: David T. Carr, M.D.—Rochester

Surgical Fate of Ureteral Stones: Lithotomy or Manipulation

William L. Furlow, M.D.—Rochester

Ileal Loop Substitute in Ureteral Injury—Case Report

Edward J. Richardson, M.D.—St. Paul

Closed Hemorrhoidectomy

Stanley M. Goldberg, M.D.—Minneapolis

Hepatic Injury and General Anesthesia

William H. Summerskill, M.D.—Rochester

Hysterical Repression of Pregnancy and Ensuing Infanticide

Dale W. Gullledge, M.D.—Rochester
Edward Litin, M.D.—Rochester

Surgical Treatment for Pulmonary Emphysema

W. Spencer Payne, M.D.—Rochester

Intravascular Coagulation in a Newborn—Case Report

Loren N. Vorlicky, M.D.—Edina

Subcutaneous Mastectomy

John Simons, M.D.—Rochester

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Book Reviews

Some books, like the City of London, fare the better for being burned.—Tom Brown

INTERNATIONAL SYMPOSIUM ON THE NUCLEOLUS: ITS STRUCTURE AND FUNCTION—National Cancer Monograph 23 (December 1966). Edited by W. S. Vincent, and O. L. Miller, Jr. Published by U. S. Department of Health, Education, and Welfare, National Cancer Institute, Bethesda, Maryland. Text 574 pages, subject index 21 pages, and 57 plates. Price \$5.00.

The monograph is a collection of papers presented during the international symposium on the nucleolus at Montevideo, Uruguay, December 5-10, 1966. Thirty-five scientific talks were given; to mention a few: "Ultrastructural aspects of the normal and pathological nucleolus in mammalian cells," "Mode of formation of the nucleolus in plant cells," "Detection and origin of nucleolar components," "A model for ribonucleic acid function," "Nucleolar enzymes," and "Ribosome biogenesis."

Over-all theme of the symposium covered nucleolar desoxyribose nucleic acid, ribonucleic acid, proteins, and structure of the nucleolus. Desoxyribose nucleic acid appears to exist in the nucleolus in form of a tangled filament. The 18S ribonucleic acid is synthesized in the nucleolus rather than in the cytoplasm. About 80-90 per cent of the dry matter of the nucleolus is protein, a considerable fraction of which is ribosome-like.

Eight structural components of the nucleolus were presented: (1) Particulate components as seen under the electron microscope, (2) fibrillar components considered aggregates of protein, (3) amorphous components most likely to be proteins, (4) desoxyribose nucleic acid demonstrated by autoradiography, (5) nucleolonema predominantly composed of R N P as demonstrated by histochemical methods, (6) vacuoles which may contain proteins, ribosomes and other substances, (7) nucleolus-associated chromatin which is probably a random assortment of chromosomal material precipitated onto the nuclear surface, (8) perinucleolar structure, an as yet hypothetical membrane awaiting future studies.

It may be summarized that the nucleolus should not be considered a simple organelle with a single function, namely, the manufacturing of ribosomes, but rather a structure through which different materials flow, a processing area of several types of ribonucleic acids, proteins from one precursor to another till they leave the nucleolus through the nucleoplasm into the cytoplasm.

The Report of the Nucleolus Nomenclature Committee is given in the Appendix.

Emil M. Schleicher, Ph.D.
Minneapolis, Minnesota

DIABETES FOR DIABETICS. George F. Schmitt: Diabetes Press of America; Miami, Florida, 1965.

"Diabetes for Diabetics" is a pocket-sized, slim, hard-cover treatise written for the diabetic patient. It contains detailed descriptions of diabetic therapy with many illustrations in color. Any literate adult could guide himself to the proper use of prescribed insulin by following the careful directions given by Schmitt. Probably an illiterate patient could do the same, by following the numerous pictures. There are also quite a number of color illustrations of food and kitchen items that are pretty to look at but of questionable value. In this category are pictures of a plastic teaspoon, a tablespoon, a can of soup, a tin of pork and beans. Any physician reading this book aimed at the lay public must temper his criticisms of a work not designed for his perusal. The public, however, deserves to be accurately informed. I question this "physiological" explanation of polyuria: "the kidneys have to remove the excess of unburned glucose; since the urine can only dissolve a certain amount of glucose, more urine must be passed." The statement "his life expectancy (the diabetic's) is approximately the same as others" is more optimistic than the facts permit. The statement "if he (the diabetic) disregards proper advice, he takes the risk of complications affecting the eyes, heart, kidneys, and nervous system" is true enough but implies that if he follows proper advice he does not assume these risks, an unwarranted implication. Several of these complications develop whether or not the patient is well controlled. However, these are minor irritations that probably will disturb only physicians and medical students who in any case will not use this work as a source of information. The diabetic patient can learn much about his disease from Schmitt's book and may achieve considerable reassurance, albeit reassurance not necessarily based on fact.

Reuben Berman, M.D.
Minneapolis, Minnesota

The college contribution

is a two-
way street



There are two ways to look at it.

There's the contribution the colleges make to business.

That's crucial.

Business employs about 42% of all college people. It uses their brainpower and skill in developing new products and methods. It fills management posts.

In the other direction, there's the contribution business makes to colleges.

The colleges welcome it. They need all the funds they can get. They're helping to prepare leaders for management, but the cost of education is going up.

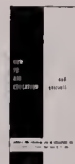
In fact many colleges are having to turn away applicants—100,000 a year, says one estimate.

If business wants college talent, it must keep colleges in business. It can help finance their need for classrooms, facilities and especially teachers.

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College is Business' Best Friend



Abstracts, Briefs and Commentaries

Aspirin and Von Willebrand's Disease*

Few know more about diagnosing bleeding diseases than Armand J. Quick. He conceived the prothrombin time in the thirties, pioneered its clinical use, has written scores of papers on coagulation, and ranks as an international authority on blood clotting.

Recently, then, when Doctor Quick wrote on how to diagnose Von Willebrand's disease with aspirin, I read closely what he had to say.^{1,2} For if one excludes the hemophilias, this is probably the commonest congenital bleeding disease. Yet many physicians have never recognized a case. Why? One reason may be that they neglect the bleeding time. In *most* patients with the disease, this crucial test is prolonged. I emphasize "most" because some patients with known disease have normal bleeding times.

In these patients, Doctor Quick uses aspirin for diagnosis. He takes a patient who bleeds abnormally, does an ear bleeding time, gives the patient two five-grain aspirins, waits two hours, and repeats the bleeding time. This he calls an aspirin tolerance test. If the first bleeding time lasts for three minutes or less, the second extends five minutes or more, and the patient has a family history of bleeding, Doctor Quick diagnoses Von Willebrand's disease.

At least that is how I interpret his facts. He took students, measured their bleeding times before and after aspirin, and found a slight prolongation of bleeding time in more than half. Then he did the same with six patients—a young man and his two sisters, and a mother and her two daughters—in whom he suspected Von Willebrand's disease. Before aspirin, bleeding times of four of these patients were 3, 3.5, 3, and 3 minutes, all borderline values; after aspirin, their times were 6.5, 10, 5.5, and 7 minutes.

From this little experiment he concluded the aspirin tolerance test "makes it possible to detect mild cases in which basic bleeding time is normal . . . the basic abnormality appears to be the lack of a factor that is further depressed by aspirin."

Richard L. Reece, M.D.
Minneapolis, Minnesota

Quick, A. J.: The Duke Bleeding Time. *Amer J Clin Path*, 47:459, 1967.

Quick, A. J.: Salicylates and Bleeding; the Aspirin Tolerance Test. *Amer J Med Sci* 252:265, 1966.

*See page 1334.

THE BLOODY NOSE*

It should be reassuring for parents to know that nosebleeds during childhood, puberty, and adolescence are rarely serious. Mothers can often control the bleeding by pressing the child's nostrils together for about 10 minutes and applying cold compresses.

Nosebleeds in elderly persons can be severe because of high blood pressure and hardening of the blood vessels. Treatment for these is best done in a hospital and consists mainly of packing the nostrils and ligating blood vessels.

Even if the bleeding is severe and prolonged, it should be comforting for the public to know that it rarely causes death.

Nosebleeds seldom result from deficiencies in the clotting mechanism of the blood.

O. Erik Hallberg, M.D.
Rochester, Minnesota

*Given before a meeting of the Minnesota State Medical Association, Duluth, May 15 to 17, 1967.

THE DISCHARGING NIPPLE*

Abnormal secretions from the breast may be defined as any nipple discharge unrelated to pregnancy. Such abnormal breast secretions, whether they are bloody or clear, may indicate the presence of a breast cancer and, therefore, can never be dismissed lightly.

The causes of abnormal breast secretions include benign tumors, inflammation, hormonal factors, certain drugs including various tranquilizers, local stimulation, injury, and various forms of breast cancer. Fortunately, most abnormal breast secretions are due to benign factors, but the burden of proof is always on the physician.

The methods for making an accurate diagnosis of abnormal nipple discharges were presented. When surgical removal of a portion of the breast is necessary for diagnosis, an adequate operation can be done with good cosmetic results. Doctor Anderson condemned the surgical removal of the entire breast without a specific diagnosis of cancer, except in the male. The higher incidence of breast cancer in the male with a true nipple discharge and the cosmetic insignificance of removal of the male breast justified mastectomy in the male for diagnostic purposes in many instances.

David P. Anderson, Jr., M.D.
Austin, Minnesota

*Summary of presentation made during annual meeting of the Minnesota State Medical Association, Duluth, Minnesota, May 15, 1967.

THE INTENSIVE CARE UNIT—CAN THE COMMUNITY HOSPITAL AFFORD IT?*

Coronary heart disease is the greatest single cause of death in the United States. Over a million people die annually, half of these despite standard hospital treatment. Eighty per cent of all deaths are due to arrhythmias, cardiogenic shock or congestive heart failure. These lethal complications arise suddenly but seldom without warning signs. Early treatment of arrhythmias and arrhythmic-induced shock and congestive heart failure is dependent on prompt diagnosis. The use of continuous EKG monitoring can prevent many of these fatal complications.

*Summary of panel presentation, Minnesota State Medical Association Meeting, Duluth, Minnesota, May 15, 1967.

It remains for each hospital staff to evaluate the magnitude of the problem in its community. Larger hospitals (300 beds or more) will probably find it feasible to establish a fixed area, coronary care unit. If interne and resident coverage is not available, highly specialized coronary care nurses must be trained and regularly drilled in fundamentals of cardiopulmonary physiology, EKG pattern recognition, emergency treatment, cardioversion, and general nursing techniques.

Smaller hospitals will find the portable monitoring systems with rate alarms more economical and practical.

All hospitals must have emergency cardiac resuscitation equipment, and the staffs must assume the responsibility of training resuscitation teams.

Physicians responsible for the establishment of such units and teams in the community hospital must realize that a program requires some hardware (electronic monitoring equipment with a defibrillator) and much software (cardiac nurse specialists, training programs) if success is to be achieved.

W. J. Henke, M.D.
St. Paul, Minnesota

PAINFUL FEET*

A practical short presentation for surgical correction of painful foot conditions is presented to the Doctors' Assembly by a practicing orthopedic surgeon. Six of the seven conditions of the feet, surgically correctable, have visible abnormalities that can be seen by anyone. Many of these enlargements, calluses, or nail deformities are aggravated by footwear.

The purpose of this discussion is to show interested surgeons what they might do to help ailing feet and to show all physicians what surgery of the foot can accomplish for their patients. Interested surgeons can learn the techniques without difficulty and help the majority of patients with these common conditions. More involved procedures may be reserved for the orthopedic surgeon.

Bunions are ordinarily most troublesome in women because of the tight fit of the shoe to keep it on the foot. Removal of the mass on the inside of the great toe and removal of a portion of the bone of the toe will create a false joint. This new joint will permit the toe to straighten and relieve pain from motion and from pressure of footwear.

Infected or uninfected *ingrown toenails* may be improved or eradicated by simple removal of tissue on the lateral borders of the involved toe. Such toe removal would include all parts of the nail down to the root. This conservative and effective measure is presented to counter the more painful and long-healing measure of removal of the whole nail itself.

Bent toes, *hammer toes*, claw toes may be corrected by division of tendons or by removal of the most prominent bone under the callus. A callus may develop around the fifth toe opposite the bunion position. This is called a *bunionette*. Here again, removal of underlying bone is effective for relief.

The one painful condition, not visible to the patient or the surgeon, is the pinched nerve or *Morton's toe*. This nerve irritation causes burning, cramping, and alters sensation at the foot near the third and fourth toes. It is worse on activity and weight-bearing. It is relieved by rest and removal of footwear. On removing the shoe, the patient massages the foot for relief. Again, application of the shoe with walking re-creates the problem. Removal of the nerve deep in the web between

*Presentation made during annual meeting of Minnesota State Medical Association, Duluth, Minnesota, May 15, 1967.

Continued

the third and fourth toe relieves the problem.

Procedures may be carried out under local or general anesthesia. The volume of local anesthesia is to be kept to a minimum. Medications which constrict the blood vessels are not used in the foot.

The surgeon performing these simple measures will add to the comfort and happiness of many of his patients. Each locality should have at least one doctor interested in surgery of the forefoot.

Kenath H. Sponsel, M.D.
Minneapolis, Minnesota

THE BUZZING EAR*

Tinnitus is the term applied to the noises heard in one or both ears by a patient when no extraneous sounds are audible. In most cases the cause is due to degenerative processes in the cochlea of the inner ear. When this is the case, no treatment is of much value, even though the noise can become severely irritating to the patient.

At times, however, the noise is a symptom of a condition which should be investigated. Conditions such as certain drug overdoses, brain tumors and dangerous narrowings in the blood vessels to the head will cause characteristic noises in the ear. Other correctable conditions of the ear will often produce tinnitus as an early symptom.

For these reasons, the individual suffering from an annoying ear noise should be fully examined to determine the cause. For those fortunate people in which a correctable condition is found, early treatment in some can often reverse a potentially lethal process; while in others, hearing loss can be prevented. For those with inner ear conditions which cannot be treated effectively, the physician can offer supportive therapy to help make the patient less aware of the noises during the quiet periods of the evening and night when these noises are most irritating. For those with severe tinnitus, use of a clock radio at bedtime is very helpful in allowing the patient to fall asleep with music blocking out the head noises.

Barclay M. Cram, M.D.
St. Paul, Minnesota

*Presentation made during Minnesota State Medical Association Meeting, Duluth, Minnesota, May 15, 1967.

AMNIOTIC FLUID EXAMINATION AND EARLY DELIVERY FOR ERYTHROBLASTOSIS.*

With modern methods of management most babies suffering from erythroblastosis fetalis may now be saved. In former years erythroblastosis fetalis, a condition caused by antibodies forming in an Rh-negative mother's blood against the red cells of her unborn Rh-positive baby, was fatal in 50 per cent of cases. Although treatment with replacement of the affected baby's blood with Rh-negative blood has been highly effective for 20 years, it has been of no avail for the 25 per cent of erythroblastotic babies who die of their disease before delivery.

Early delivery has been practiced with success in Winnipeg for the past 13 years but is dependent upon the accurate prediction of severity of erythroblastosis before the baby is born. Until recently, history of previously affected babies and the strength of the antibody in the mother's blood were the only means of determining

*Summary of presentation in the panel on Erythroblastosis, Minnesota State Medical Association Meeting, Duluth, Minnesota, May 16, 1967.

how sick the baby was. These two indicators were only 62 per cent accurate in predicting severity of disease.

Optical Density

With the addition of amniotic fluid examination accurate prediction of severity of erythroblastosis in the unborn baby has risen to 95 per cent. Amniotic fluid, the fluid in which the baby floats, is swallowed and voided by him. The test used to determine severity of disease in the fetus involves removal of a small amount (two teaspoons) of amniotic fluid through a needle inserted under local anesthetic through the pregnant mother's abdomen into the uterine cavity. The fluid is protected from light which destroys its usefulness and is examined in a spectrophotometer. Optical density readings are made at various wave lengths and a measurement of the increase in optical density at the wave length 450 m μ is made. It is this increase in optical density which mirrors the severity of erythroblastosis. These measurements have been a great help in determining which women have babies so severely affected with erythroblastosis that they must be delivered early for any hope of survival and which women have babies which may safely be left to deliver at term. On the basis of an aggressive policy of early delivery in selected cases of erythroblastosis in the past four years 59 women in Winnipeg have had their babies delivered six or more weeks before their expected dates. Forty-eight of the 59 have had surviving babies. Seven of the 48 have come from the United States.

Amniotic fluid examination has also proven of great value in selecting the one sensitized Rh-negative woman in 12 whose unborn baby will die so soon that early delivery is valueless and in whom pre-birth intra-uterine transfusion must be undertaken.

John M. Bowman, M.D.*
Winnipeg, Canada

*Clinical Director, Rh Laboratory, Associate Professor Paediatrics, University of Manitoba.

THE INTENSIVE CARE UNIT—CAN THE COMMUNITY HOSPITAL AFFORD IT?*

With the advent of Intensive Care Units in hospitals there must be a re-evaluation of the possible and potential legal exposure that hospitals and doctors may face by way of claims by patients that have been placed on intensive care in these units.

It should first be recognized that the modern trend of courts and juries has been to put a greater responsibility in general on hospitals as to the care that they expect to receive in all phases of hospital treatment.

The addition of the Intensive Care Unit to hospital services can present unique problems from a medicolegal standpoint. The very title, incorporating the words "Intensive Care," seems to beg for a claim by the public and particularly by a patient demanding: "Did I receive intensive care?" We must therefore explore this potential legal problem of additional claims and decide what efforts can be made to avoid them.

It is suggested that physicians can do much to alleviate the problem by using their office as hospital staff members to be sure that the nursing staff and hospital per-

*Presentation given during annual meeting of Minnesota State Medical Association in Duluth, Minnesota, May 15, 1967.

Continued

sonnel are adequate in number and properly trained. Some hospital staffs have seen fit to place the Intensive Care Unit under the Department of Anesthesiology, thereby centralizing the responsibility for the operation of the unit.

As attending physicians, the members of the medical profession can also do much to protect themselves and the hospital by proper education of their patients and patients' families about the function of the Intensive Care Unit and the necessity therefor. It seems imperative that when a physician puts a patient in an Intensive Care Unit, he himself assume added responsibility to be more detailed in the orders given and satisfy himself at frequent intervals that those orders are being complied with. It is further suggested that the attending physician familiarize himself with the nursing personnel on duty and work closely with that personnel on a teamwork basis.

There is a concerted effort at the present time to bring the Intensive Care Unit to the small community hospital, especially in the area of cardiac care units. Since the problems confronting the small community hospital will be essentially the same as those confronting the large metropolitan hospital, many of the problems may be more difficult to resolve because of lack of sufficient trained personnel. The establishment of the Intensive Care Unit in a small community hospital will obviously place a greater burden on the smaller staff of physicians available for supervision of the unit, thus requiring greater cooperation from the local physicians to guarantee successful operation of the unit.

With the rapid development in medical technology it is difficult to see how a large hospital can afford to be without an Intensive Care Unit, and it is certainly desirable for the small community hospital to have such a life-saving unit available. However, we must at all times recognize the potential legal pitfalls confronting the hospital and its staff if the unit is not properly managed and operated.

Jerre F. Logan*
Attorney
Minneapolis, Minnesota

*Tyrrell, Jardene, Logan and O'Brien Law Offices

Seasonal Diseases

The diseases of *spring* are, maniacal, melancholic, and epileptic disorders, bloody flux, quinsy, coryza, hoarseness, cough, leprosy, lichen albus, exanthemata mostly ending in ulcerations, tubercles, and arthritic diseases.

Of *summer*, certain of these, and continued, ardent, and tertian fevers, most especially vomiting, diarrhea, ophthalmia, pains of the ears, ulcerations of the mouth, mortifications of the privy parts, and the sudamina.

Of *autumn*, most of the summer, quartan, and irregular fevers, enlarged spleen, dropsy, phthisis, strangury, lenteria, dysentery, sciatica, quinsy, asthma, ileus, epilepsy, maniacal and melancholic disorders.

Of *winter*, pleurisy, pneumonia, coryza, hoarseness, cough, pains of the chest, pains of the ribs and loins, headache, vertigo, and apoplexy.

—Hippocrates

The only thing everybody understands about money matters is that it does.

—Changing Times

A large, dark, grainy microscopic image showing numerous spermatozoa. The sperm heads are visible as bright, oval shapes, and their long, thin tails (flagella) are seen as wispy, hair-like structures extending from the heads. The background is dark and textured.

New view of an oral contraceptive at work

Although suppression of ovulation remains the primary mode of action of oral contraceptives, newer knowledge indicates that products like Norinyl-1 — a combination of both low-dosage progestogen and estrogen for the full treatment cycle — may provide multiple action that helps explain their unexcelled record of contraceptive effectiveness. This report explores the possible secondary protective mechanisms offered by combined hormonal administration.

Accumulating evidence has indicated that sparse, highly viscous cervical mucus has a possible adverse effect on the motility and survival of spermatozoa.

The estrogen-opposing progestational ingredient of Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.) changes the usual mid-cycle picture of a thin, watery cervical mucus. The result — a built-in barrier that appears to inhibit sperm from reaching the ovum should one be released. The inset in the adjoining photograph shows immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

How the estrogen-opposing action of Norinyl-1 creates cervical mucus that may be hostile to sperm penetration

Normally, estrogen activity during the fertile midcycle stimulates the production of a profuse and watery cervical mucus that permits maximum sperm motility and promotes penetration.

But what happens when Norinyl-1 is administered? Its potent progestogen, norethindrone, opposes estrogen stimulation of cervical mucus. Consequently, the amount of mucus decreases and its viscosity increases. This results in a sparse but thick mucus barrier that appears to diminish the vitality of the sperm and to impair its powers of penetration.

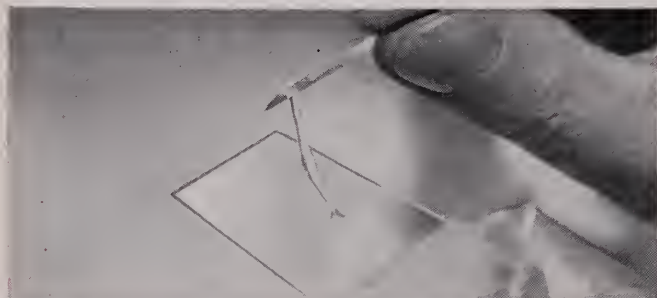
The role of viscous cervical mucus as a secondary action of Norinyl-1

In a report on 89 patients taking this medication,* cervical mucus obtained from cycle day 5 to cycle day 29 appeared scant and thick and exhibited little or no Spinnbarkeit.

In the opinion of this investigator, the effect on cervical mucus may be sufficient to prevent conception.

*Cohen, M. R.: Symposium: Mechanisms of Action of Low Dosage Oral Contraceptive, Yale University Medical Center, New Haven, Conn., April 6, 1967.

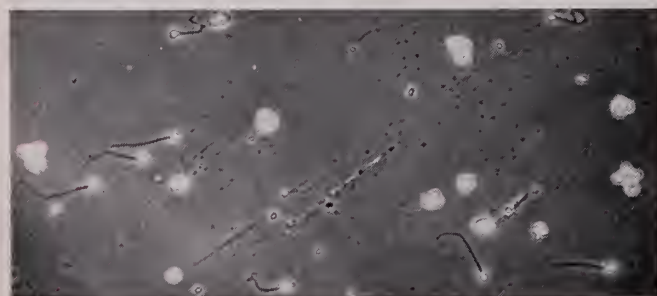
Normal cervical mucus at midcycle in untreated patient is known to permit sperm motility... promote sperm penetration.



Cervical mucus is thin and watery with a stretchability (Spinnbarkeit) of 15 to 20 cm.

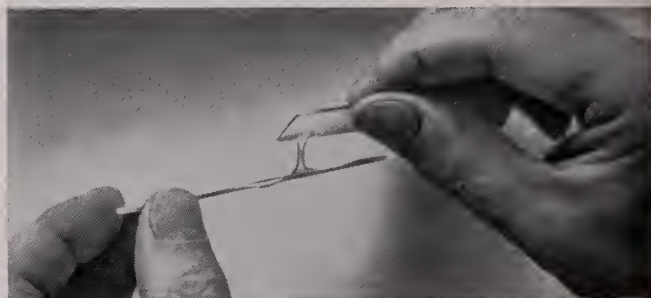


Thin, watery mucus crystallizes into this well-defined, fernlike pattern within a minute.

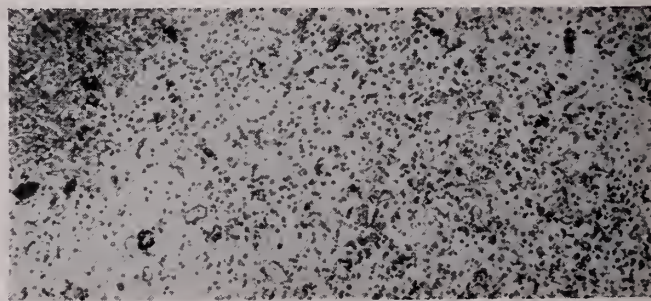


Spermatozoa appear healthy, are active and freemoving.

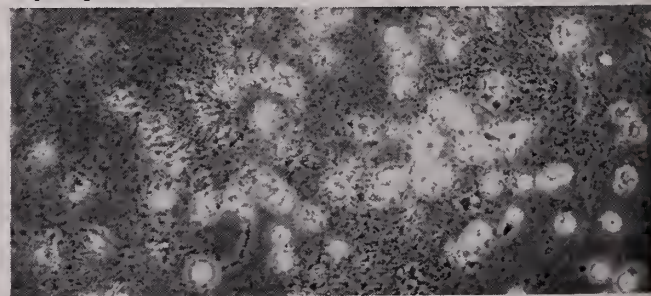
Viscous cervical mucus at midcycle produced by Norinyl-1 appears to impair sperm vitality... inhibit penetration.



Cervical mucus is scanty, thick and viscous. Spinnbarkeit is 1 cm. or less.



In thick, viscous cervical mucus the fern pattern is poorly defined or absent.

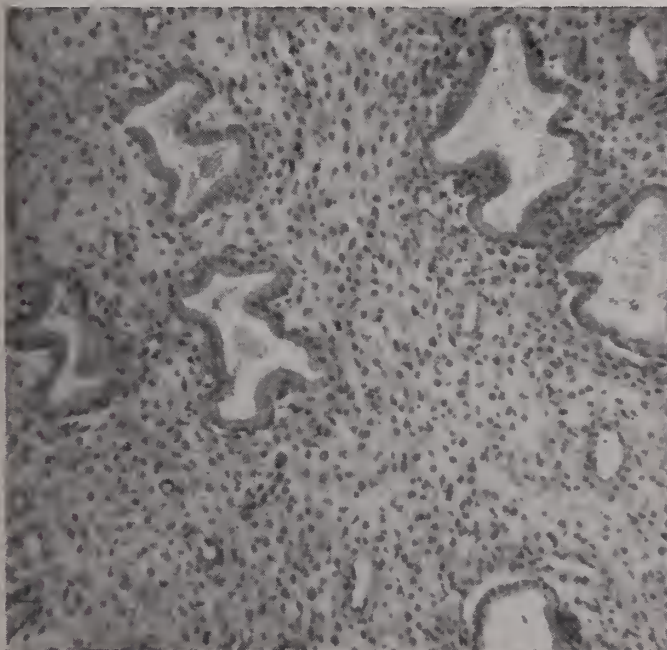


Immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

How Norinyl-1 alters normal endometrial responses— another possible protective mechanism

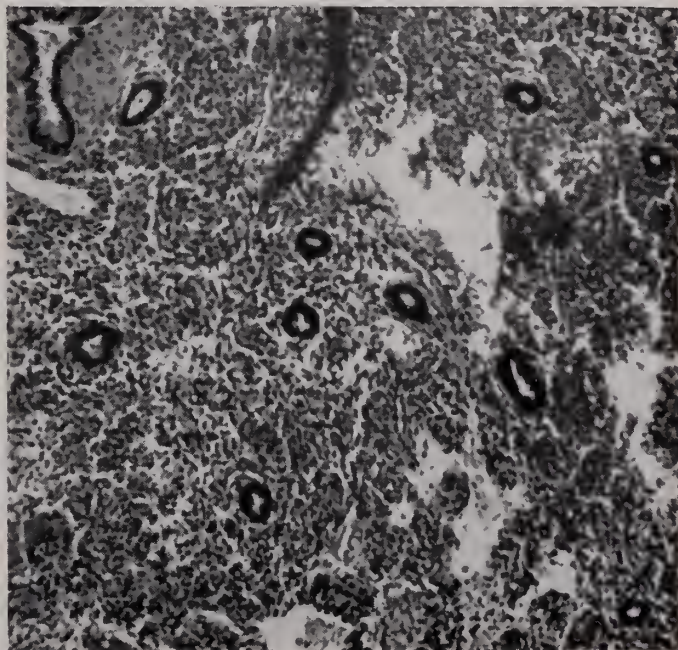
Let us suppose that an ovum is released—as occurs in an occasional, rare case—and somehow a sperm succeeds in penetrating the cervical mucus barrier. Should this come about, one additional action of Norinyl-1 may protect the patient from unwanted pregnancy. The theory is that progestogen intake makes endometrial tissue unreceptive to implantation.

Endometrium of
untreated patient



Normally, the endometrium progresses through a proliferative phase stimulated by estrogen and a secretory phase stimulated by progesterone. During the secretory phase the endometrium is receptive to the fertilized ovum.

Endometrium produced
by Norinyl-1



When Norinyl-1 is administered its progestogen component—norethindrone—accelerates the secretory phase and suppresses glandular and vascular development.

effective fertility control
on half the previous dosage
maintains ratio
of the established
norethindrone/mestranol
combination
lower cost

new Norinyl-1[®] tablets

(norethindrone 1mg. $\bar{c}$ mestranol 0.05mg.)

Reduction of oral contraceptive dosage to lowest effective levels has become a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now available in a new strength in which both norethindrone and mestranol are reduced 50 percent. Studies show that Norinyl-1 achieves fertility control with only 1.05 mg. of combined progestogen and estrogen per tablet.

Norethindrone was first reported for use as a progestational agent in human beings in 1955. Norethindrone 2 mg. with mestranol 0.1 mg., as an oral contraceptive, is currently in use by over 2,000,000 women. Clinical experience now establishes that Norinyl-1 also amply meets the criteria of reliability and safety.*

*Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965.

PRESCRIBING INFORMATION

Contraindications: 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

Warnings: 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of Norinyl-1 in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

Precautions: 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with Norinyl-1. Therefore, if such tests are abnormal in a patient taking Norinyl-1, it is recommended that they be repeated after the drug has been withdrawn for 2 months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibroids may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac, or renal dysfunction, require careful observation. 5. Although a cause and effect relationship has not been established, Norinyl-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, as in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are

indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged Norinyl-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Norinyl-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. A cause and effect relationship has not been demonstrated. 11. Because of the effects of estrogens on epiphyseal closure, Norinyl-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask the onset of the climacteric. 13. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

Side Effects: The following adverse reactions have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma, breast changes (tenderness, enlargement and secretion), loss of scalp hair, change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, erythema multiforme, erythema nodosum, hemorrhagic eruption, migraine, rash (allergic), itching, rise in blood pressure in susceptible individuals, mental depression.

The following occurrences have been observed in users of oral contraceptives. A cause and effect relationship has not been established: thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory results may be

altered by the use of oral contraceptives: increased bromsulphalein retention and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in T₃ values), metapyrone test, pregnanediol determination.

Other side effects reported to have occurred in association with use of this drug are dizziness, hirsutism, pains in legs, back, chest and abdomen, dysuria, drowsiness, vaginal discharge, libido increased and decreased, eruptions, hypermenorrhea, hypomenorrhea, increased appetite, G.U. infections, varicose veins, abdominal fullness, acne, headache, nervousness, allergies, blurred vision, pain in eyes, and itching in eyes. For complete clinical data, see package insert.

Dosage and Administration: 1. One tablet of Norinyl-1 is administered orally for 20 days beginning on day 5 of the menstrual cycle. (Count day 1 of the cycle as the first day of menstrual bleeding.) Repeat this dosage schedule for each cycle. 2. If no menstrual period occurs after a cycle of treatment (20 tablets) in which patient adhered to the schedule, the patient must be instructed to resume taking the Norinyl-1 tablets 7 days after the previous 20-day course was completed. For example, if the last pill of a previous cycle had been taken on a Sunday, then a new cycle of treatment should begin on the following Sunday. 3. In the postpartum woman, it is recommended that the first cycle of treatment should begin on day 5 of the first menstrual cycle. However, Norinyl-1 should not be administered during lactation.

Availability: Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.)—Dispensers of 20 and 60 and bottles of 250 tablets.

norethindrone — an original steroid from
SYNTEX
LABORATORIES INC., PALO ALTO, CALIF.

Special Article

What of Tomorrow?*

OWEN H. WANGENSTEEN, M.D.**
Minneapolis, Minnesota

Your Outlook and Opportunity

TRADITIONALLY the significant occasions in our lives are birth marriage, and death. To these I would add graduation, signaling entrance upon life's tasks.

This is a moment to which you and your families have looked forward for a long time. There have been years of planning and saving. Days of frustration and disappointment too, with interspersion of inspiration and crystallization of hopes. You present testimony as well as evidence that a medical school is a place where medicine is studied as well as taught. While you are now definitely on your way, only a beginning has been made.

A century ago, Sir James Paget,¹ a well known British Surgeon-Teacher, remarked to a graduating medical class—"What will become of you?" The pattern of Paget's day probably remains the same today. I know the work of a number in this class well enough to believe that many of you are destined for careers of unusual distinction, whether in practice in a small or large community or in the advancement of a discipline. Many of you will become Teachers and regale your own professional children with progressive extensions of the lessons you have put to a good account. Some of you may become Casanovas of the inkwell unless an early case of authors' lead poisoning persuades you to desist.

The promise of success can be foretold most accurately by the spirit of your dedication and motivation. In this life one can have almost anything he wants, granted he wants it enough to

work for it in and out of season. The difficulty is that our wants are so many and it is so easy to equate want with need. Between these, as Leon Tolstoy indicated, and as many learn only too late, there is a significant difference. Our needs actually are few. Our wants are limitless. He who wishes to succeed at everything may become a very versatile person but is unlikely to acquire distinction in many or any of those interests. The best known aphorism of Hippocrates is that art is long and the acquisition of learning difficult. In order to succeed, one must be ready to accept Hippocrates' wisdom as a guideline. Obviously, Hippocrates did not write those sage words as a young man.

The outlets for the young physician are numerous. Fortunate is he who decides early in his career what he would like to do and then marches slowly, relentlessly, and without interruption toward its achievement. It is not the goal itself, but the struggle toward its achievement that constitutes the true reward.

The real paymaster of any of us is opportunity—to serve, create, improve and relieve. Those of you who enter active practice and are willing to walk this trail with no desire other than to bring healing and relief from suffering to your patients will encounter a depth of gratitude not surpassed by any other type of remuneration.

If I had Fortunatus' wishing cap and could grant you three wishes, I would wish you great enthusiasm for your work, a spirit of industry and consecutiveness, accompanied by an appreciation of and love for your fellowman. With these compelling incentives, you could not fail no matter where life's adventure takes you.

Continuing Fission of Biologic Disciplines

During my earlier years in surgery, by spend-

Continued

*Presented at the University of Minnesota Recognition Program honoring the Senior Class in Medicine, Friday, June 9, 1967.

**Department of Surgery, University of Minnesota Hospitals, Minneapolis, Minnesota.

ing every Saturday afternoon in the library, I could gain a nodding acquaintance with all the current surgical literature of the world. Today, if a young surgeon read every waking minute he could not begin to do this. After acquiring a broad background of training in the discipline of one's election, it is necessary to concentrate on a smaller field to acquire some suggestion of expertise. A challenging summons comes also from the Public to get on with medical research in quest of better solutions of present-day problems.

Instruments of Precision

A century ago, instruments of precision brought new medical disciplines into being; witness the cystoscope, ophthalmoscope, otoscope, laryngoscope. Roentgen's great discovery (1895) made a terrific impact upon 20th Century medicine, as did the birth of microbiology and knowledge of infection a few decades earlier. The present continuing fission of biological disciplines reflects essentially a conflux of archipelagos of ideas converging into peninsulas of information, thus creating by mitosis and fusion new biologic systems from which the Profession and the Public may rightfully look to virgin techniques accelerating significant new developments.

I have the boldness to believe that the biologist-historian, by studying extending peninsulas of knowledge in the interphases between biologic disciplines, with the help of librarians and interested biologists in the disciplines involved, can speed discovery and lend meaning to knowledge. One need only think back upon the significant preludes to Lister. Many had written that antiseptic management of wounds saved life and diminished or precluded suppuration of wounds, but little note was taken of their publications until patrols and later armies of microbes were marshalled onto the scene to support their position.

Extra-Corporeal Oxygenation

The most exciting development in Surgery during my tenure has been that of intracardiac surgery, much of the history of which was written here. All of you have been witnesses to this development. What you must appreciate, however, was the importance of the background of training for the men who gave impetus to this development. Techniques of oxygenating the heart without lungs were long known to students of the circulation. When, however, surgeons

trained in physiologic techniques and with dedication matched by imagination and courage, undertook exploration of the problem, this combination made the venture a great success. For a period of more than 30 years, with the helpful cooperation of colleagues in other disciplines, and particularly with M. B. Visscher, Professor of Physiology, it has been the objective of the Surgery Department to see to it that every surgeon with academic aspirations has a training in a basic medical discipline.

Students of tissue transplantation will need orientation in many fields, notably genetics, radiology, and pharmacology to overcome the disturbing factors of antigenicity and incompatibility which now stand in the way of its progress.

Metchnikoff, Methuselah and Prospects for Prolongation of Useful Life

"From 20 to 50 man should live for himself and his family; from 50 to 100 for science and humanity, and after a hundred for the State. . . . We should live till 140 years of age."

Three Score and Ten

Some of you may infer that these words were born in the mind of a current visionary. I hasten to add that Elie Metchnikoff² authored that dreamy prediction in 1903 when he was 58; he died at 71. The Biblical seers understood better the promises of old age than did Metchnikoff or modern prophets who are fond of predicting useful lives to 100. The 90th Psalm reminds us that "the years of man are three score and ten and if by strength they be four score years, yet is their strength but labor and sorrow." It has been my privilege and obligation over long years to have had much to do with persons in the 9th decade of life. Without exception, they want to continue their existence as long as they find the company of their associates reasonably acceptable. Occasionally one meets a person who is strong in body and mind in his late 80's, but such are few indeed. Methuselah's only distinction, apart from being Noah's grandfather, was his age. Methuselahs are currently not popular in any market and make no appeal in the marriage mart either, unless accompanied by a substantial bank account.

The Library, Books and Reading

High on the agenda of the needs of this Medi-

cal School during my tenure was a biomedical library. The pressure of other necessities pushed it aside for many years. Your class has been amongst the first to have the advantage of ready access to a fine collection of books. In books one finds his life influenced by great teachers of the past. Many of you have probably observed on a wall of our Surgical Conference Room the nice incentive to reading by Anthony Trollope³ (1862): "With reference to the habit of reading, I make bold to tell you it is your pass to the greatest, the purest and the most perfect pleasures that God has prepared for his creatures. . . . When a young man looks into a girl's eye for love, and finds it there, nothing may afford him greater joy for the moment: When a father sees a son return after a long absence, it may be a great pleasure for the moment: But the habit of reading is the only enjoyment I know, in which there is no alloy. It lasts when all other pleasures fade."

Pressures of the Expanding Curriculum

It is unfortunate that in our schools the pressure of examinations often forces the student to concentrate on examinations rather than to increase his stores of knowledge. It has long been my view that if all the disciplines from anatomy to zoology were taught from an historic point of view, emphasizing those items which survived the erosion of time, our medical students would be better informed. It will interest you to know that the text books in surgery recommended to the first graduating class in medicine from this School 75 years ago were as large as those of today. Yet, surgery of the great vessels and the thorax, including the lung, heart and esophagus, as well as the cranium, was unknown. The truth of the matter is that much of what is taken for gospel truth in many current-day textbooks just is not so, as future enlargements of knowledge show.

Preparation for Practice

Samuel Johnson⁴ said, in advising a native Virginian contemplating the study of medicine abroad: "The Scotch like a house built to last a man's lifetime only. The English like a palace or fortress intended to last many ages. The first build lightly, the last lay a very strong and firm foundation

before they begin the work." We might do well to ponder the critique of Sam Johnson, who appreciated that education at Oxford or Cambridge preliminary to pursuit of conventional medical training at London in his day took approximately 14 years. If we perpetuate our present long scheme of training, we shall never recruit enough personnel to fill the ranks. More than 30 years ago Will Mayo,⁵ long a Regent of this University, believed that medical schools should begin to think of varying lengths of training for physicians.

Changing Character of Medical Practice

Today there are more physicians in the United States than there were in the entire world in 1880;^{*5a} yet there are not enough. Our Boards of Licensure have had to relax rules for admission to practice for foreigners in the interest of the needs of our people. How is this great existing demand to be met? The cry of the public is for more physicians pursuing Family Practice. Every hamlet wants its doctor.

Reduce Training Period

The only way we can have more physicians is to make the field of medicine more attractive. The training period must be reduced. Presidents, Congressmen, and business executives learn on the job and so too do University Professors. By eliminating one year in elementary school, another in high school, another in college, and by omitting the internship, the training of prospective physicians could be reduced by approximately four years. Physicians would be graduating at the age of 22 to 23 instead of 25 to 27. They could employ the salvaged time usefully in preparation for their life's work.

Family Practitioners

Are there other sources for Family Practitioners? When our Medical School began, there were two charters, one for the practice of medicine, one for homeopathy. By the year 1909, homeopathy had been dropped from the curriculum and became fully absorbed by the profession. There are probably now approximately 15,000 osteopaths in the United States. Our profession accepts them. In fact, one of the colleges of osteopathy has been converted into a full-fledged medical school. My occasional contacts with those who profess oste-

Continued

*5a. John Shaw Billings (1881) indicated there were 180,000 physicians in the world then and 65,000 in the U. S. An item in the New York Times suggests there are now more than 300,000 physicians in the U. S.

opathy would be to encourage most, if not all of their graduates to become Family Practitioners. Of the 109 osteopaths in Minnesota, only two have full hospital privileges; an additional 20 may prescribe drugs and perform minor surgery.⁶ An extension of their prerogatives could help resolve our poor showing in providing ready access in peripheral areas of our State to competent medical care. More and more patients of Family Physicians come to their offices; house calls are becoming far less frequent. So it is too in England. A recent report⁸ indicates that 85 per cent of the Family Physicians' practice in the midlands of England is performed in the doctor's office. Moreover, their Family Physicians perform only minor surgery, a trend that is growing here too. The Family Physician, in clinics and medical centers, will come to occupy a unique role between specialists and his community of patients. Osler Peterson,⁹ an ardent student of the problem of medical care and a graduate of our School, advocates reorganization and redistribution of medical care, emphasizing the need for more effective regionalization of hospital service. In such a scheme, the Family Physician too will carve out a useful niche in the Hospital Team. Medical Center Hospital practice will in time come to supersede solo office practice. Recruitment of a million paramedical people for our hospitals and medical centers would permit physicians to extend their services usefully to larger numbers of patients.

The Clinic Idea

Certainly the trend is towards specialization. The "clinic idea", to which the Brothers Mayo lent such great impetus, might well become standard practice everywhere. Directly following World War II, through the activation of the Hill-Burton Act, the Government built well equipped hospitals throughout our country. There are now 67 hospitals in Minnesota, fairly well dispersed throughout the state, that are beneficiaries of such support. In some states, notably Oklahoma,⁷ a cooperative enterprise among these community hospitals and the State University has come into being, with a studied attempt to bring in well qualified specialists cooperating fully as Teams with the physicians in the area, with other existing clinics and with the University Medical Center. An extension of this principle could bring a superior brand of medical practice into almost every area of our State.

At the Minnesota State Medical Association meeting held in Duluth in May, in chatting with practitioners whom I have known well over the years of my tenure here, I was told of increasing numbers of villages and towns in Minnesota without physicians.

Emolument

What of emolument? I am of the opinion that satisfying conditions of work constitute the best paymaster of the physician. Whereas mink coats and Cadillacs continue to be symbols of success for the business executive, the physician, with satisfying conditions of work, and the medical scientist too, whether clinician or experimentalist, does not need these ostentatious symbols of success. Their reward lies primarily in enviable opportunities, in the gratitude of patients and in the knowledge of spending their lives in the betterment of man's lot. J. Pierpont Morgan quoted St. Paul correctly when he said, it is not money but "the love of money that is the root of all evil."

Time is the most important commodity we have and whether primarily engaged in the practice of medicine, the care of patients, or in medicine's advancement, to have the opportunity of pursuing one's primary objective is indeed compensation which exceeds all others in value.

The Future

What of the future? Throughout the ages, great figures in medicine like Ambroise Paré have predicted that medicine has already reached maximal achievement. Said Paré in 1575: "Posterity will not be able to surpass us (be it said without malice or offense) save by some additions such as are easily made to things already discovered."¹⁰

Twenty-five years ago who could have foreseen the development of intracardiac surgery within a decade? Who can predict what physicians will be doing in the year 2000? Certainly many disciplines yet unknown will come into being, making this an exciting time in which to live and work.

The world has always been in a confused state. Did not Job admit that his affliction was in part confusion? If all the costs connected with the preparation for war could be expended upon man's improvement, rather than upon bringing those who oppose us to their knees, what a Utopia

this could be!

On the smaller stage of our own work, each of us by example and commitment to those objectives for which our profession stands can make our contribution to the improvement of man's lot. Was this not the Great Master's appraisal of how best to spend one's life? In your work, by enriching the lives of those whom you are privileged to serve, you repay your debt to Society for the splendid opportunity of a medical education.

Gratitude is a wonderful quality. You will recall that the physician St. Luke reminds us that the Great Master healed ten patients with leprosy but only one returned to give thanks. Scriptures tell us too that the Lord loves a cheerful giver. When you find yourselves more affluent than now, remember that the Medical School and its Minnesota Medical Foundation appreciate and understand the warm spirit of gratitude manifested by that Samaritan leper who recognized his obligation.

However much we appreciate and take pride in the accomplishments of our School, it is even more important that we cultivate a spirit of warm affection and gratitude toward it. Our School, however, is not neutral in gender but distinctly feminine—Alma Mater, our spirited foster Mother. Keep her always high in your thoughts and

affections.

In conclusion, let me remind you once more that what you wish for in youth and work for persistently with diligent perseverance, in time you will have in abundance.

A boy who grew up in the shadow of our State Capitol and who became a famous investigator and Teacher relates how his dying mother called him to her bedside to leave an instruction for his future. Said the mother¹¹ to her 10-year-old son: "Walter, be good to the World," and that Walter Cannon did, every student of Medicine and Physiology can appreciate.

Who amongst us, in standing before Northrop Auditorium, on raising his eyes to read that inscribed inscription, has not felt a warm glow and a quickening of his emotions.¹²

"The University of Minnesota
Founded in the Faith that Men are
Ennobled by Understanding
Dedicated to the Advancement of Learning
and the Search for Truth
Devoted to the Instruction of Youth and
the Welfare of the State"

Your teachers, parents, wives and husbands will want to join me now, I know, in saying to you in unison with a resounding voice: Well done and Bon Voyage!

References

1. Paget, James: What Becomes of Medical Students? Selected Essays and Addresses edited by Stephen Paget, 1902, p. 27-32 (from Longmans Green & Co., London) (reprinted from St. Bartholemew Hospital Reports for 1869).
2. Metchnikoff, Elie: The Nature of Man. Studies in Optimistic Philosophy. English Translation by P. Chalmers Mitchell. Quotation preceding Introduction "From the Times May 22, 1903, on the appearance of the French Original" Wm. Heinemann, London, 1906.
3. Trollope, Anthony: Inaugural Address on Opening of the New Mechanics Institute Exhibition in Bolton Chronicle, p. 3, December 12, 1862.
4. Johnson, Samuel: Early Letters of Arthur Lee. Southern Literary Messenger, 29:63, 1859.
5. Mayo, W. J.: Personal communication to author (Ca. 1936).
- 5a. Billings, John Shaw: Our Medical List. International Medical Congress, 1:54, 1881, London.
6. Brunn, Harold: Personal communications, May 29 and June 6, 1967.
7. Dennis, James: Personal communication, April 11, 1967.
8. British Medical Journal, and The Lancet, 1966-67.
9. Peterson, Osler L.: Medical Care: Its Social and Organizational Aspects: Evaluation of the Quality of Medical Care. New Eng J Med 269:1238, 1963.
10. Paré, Ambroise: The Works of That Famous Chirurgie of Ambrose Parey, translated out of Latin and compared with the French by Th. Johnson, London: Th. Cotes and R. Young, p. 463, 1634.
11. Cannon, Walter B.: The Way of an Investigator, New York, p. 15, 1945.
12. Inscription on Mayo Memorial, written initially by Dr. Hartley Burr Alexander and revised by Dean Guy Stanton Ford, Regent Fred B. Snyder and Professor F. M. Mann—personal communication from Mrs. Maxine Clapp, University Archivist, June 7, 1967.

Power

In the struggle for power there is no middle course between the highest elevation and the abyss of destruction.—Tacitus

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Meetings and Announcements

Iron sharpens iron; scholar, the scholar—The Talmud

SEPTEMBER

Association of Minnesota Internists Meeting, September—To be set

Scott-Carver County Medical Society Meeting, September 5, Wagner Supper Club, Jordon, Minnesota, 7:30 P.M.

Zumbro Valley Medical Society Annual Meeting, Plummer Hall, 8:00 P.M., September 6.

Minnesota-Dakota-Manitoba Orthopedic Society, Annual Meeting, Rochester, Minnesota, September 8-9 (Tentative).

Minnesota Radiological Society Annual Fall Meeting, Brainerd, Minnesota, September 9-10.

Southwestern Minnesota Medical Society Meeting, September 11, Ehlers Supper Club, 7:00 P.M.

St. Louis County Medical Society Executive Committee, St. Mary's Hospital, 6:00 P.M.—Regular Meeting, St. Mary's Hospital, 8:00 P.M., September 14.

Minnesota Academy of General Practice, AAGP Congress of Delegates, Dallas, Texas, September 16-18; AAGP Scientific Session, Dallas, Texas, September 18-23.

Hennepin County Academy of General Practice Membership Meeting, Minneapolis Athletic Club, 6:00 P.M. Social Hour; 7:00 P.M. Dinner; 8:00 P.M. Program, September 18.

Blue Earth Valley Medical Society Meeting, September 20, Interlaken Golf Club, Fairmont, 7:00 P.M.

McLeod County Medical Society Meeting, September 21.

Twin City Urologic Society Meeting, September 21, Town and Country Club, St. Paul, 6:00 P.M.

Northwestern Pediatric Society General Meeting, White Pine Inn, Bayport, 9:30 A.M. (All Day and Dinner), September 22.

Ramsey County Medical Society Regular Meeting, 1500 Lowry Medical Arts Building, St. Paul, 8:00 P.M., September 25.

Lyon-Lincoln County Medical Society Business Meeting, Chalet Club, Marshall, 6:30 P.M., September 26.

Range Medical Society Regular Meeting (Place not yet determined), 6:30 P.M., September 26.

Minnesota Chapter, American Academy of Pediatrics, September 28, Town and Country Club, St. Paul, 6:00 P.M.

Upper Mississippi Medical Society Fall Meeting, Pine Cove Inn, Wadena, 3:00 P.M., September 30.

OCTOBER

Hennepin County Academy of General Practice, October 2, Membership Meeting, Pick-Nicollet Hotel, 6:00 P.M. Social Hour; 6:45 Dinner, 7:45 Business meeting.

Hennepin County Medical Society, Pick-Nicollet Hotel, October 2, 6:00 P.M. Social Hour; 6:45 Dinner, 7:45 Business meeting, 8:15 Sectional meetings.

Southwestern Minnesota Medical Society, October 2, Ehlers Supper Club, 7:00 P.M.

Lyon-Lincoln County Medical Society, Clinical Lectures, Chalet Club, Marshall, October 3, 10, 17, 24, 6:30 P.M.

Scott-Carver County Medical Society, October 3, Wagner Supper Club, Jordan, Minnesota, 7:30 P.M.

St. Louis County Medical Society, Executive Committee, St. Luke's Hospital, 6:00 P.M., Regular Meeting, St. Luke's Hospital, 8:00 P.M., October 12.

Hennepin County Academy of General Practice Membership Meeting, Minneapolis Athletic Club, October 16, 6:00 P.M. Social Hour; 7:00 P.M. Dinner, 8:00 P.M. Program.

Minnesota Society of Internal Medicine, October 16, Rochester, Minnesota.

Blue Earth Valley Medical Society, October 18, Interlaken Golf Club, Fairmont, Minnesota, 7:00 P.M.

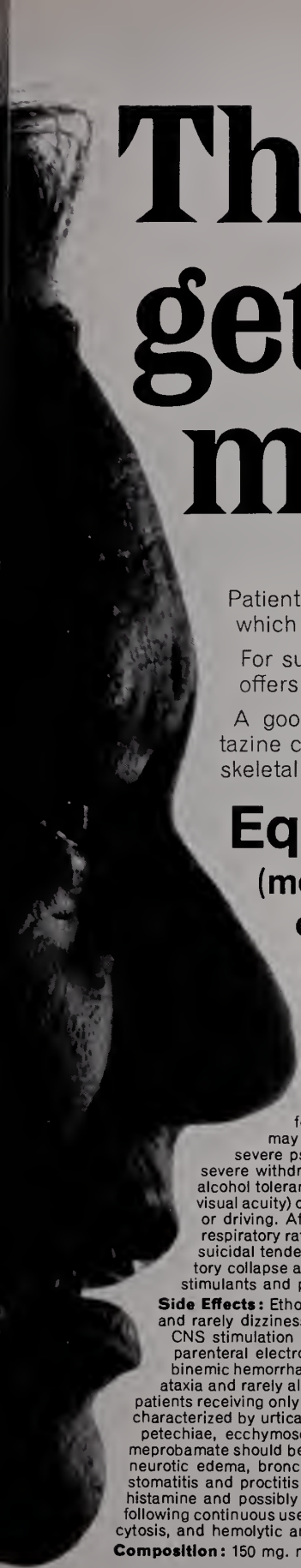
McLeod County Medical Society, October 19.

Twin City Urologic Society, October 20, Town and Country Club, St. Paul, 6:00 P.M.

Ramsey County Medical Society, Clinical Meeting (Subject to change), October 30, St. Paul-Ramsey Hospital, 8:00 P.M.

Lyon-Lincoln County Medical Society, Annual Meeting, Chalet Club, Marshall, Minnesota, 6:30 P.M., October 31.





This pain is getting on my nerves.

Patients in pain often experience concomitant anxiety and tension, which may add to the burden of pain.

For such patients, you may want to prescribe a preparation that offers more than simple analgesia.

A good choice is often EQUAGESIC® (meprobamate and ethoheptazine citrate with aspirin). It helps relieve pain. And anxiety. And skeletal muscle spasm as related to pain or anxiety and tension.

Equagesic® TABLETS

(meprobamate and ethoheptazine
citrate with aspirin)



Contraindications: History of sensitivity or severe intolerance to aspirin or meprobamate.

Warnings: USE IN PREGNANCY: Safety for use during pregnancy or lactation has not been established; therefore it should be used in pregnant patients or women of child-bearing age only when the physician judges its use essential to the patient's welfare.

Precautions: Keep out of reach of children. Not recommended for patients 12 years old or less. Carefully supervise dose and amounts prescribed, especially for patients prone to overdose themselves. Excessive prolonged use of meprobamate may result in dependence or habituation in susceptible persons—as alcoholics, ex-addicts, severe psychoneurotics. Withdraw gradually after prolonged high dosage to avoid possibly severe withdrawal reactions including epileptiform seizures. Warn patients of possible reduced alcohol tolerance. If drowsiness, ataxia or visual disturbances (impairment of accommodation and visual acuity) occur, reduce dose. If symptoms persist, caution patients against operating machinery or driving. After meprobamate overdose, prompt sleep, reduction of blood pressure, pulse and respiratory rates to basal levels, and hyperventilation are reported. Give cautiously to patients with suicidal tendencies. Treat attempted suicide (has resulted in coma, shock, vasomotor and respiratory collapse and anuria) with immediate gastric lavage and appropriate supportive therapy (CNS stimulants and pressor amines as indicated).

Side Effects: Ethoheptazine and aspirin may occasionally cause nausea, vomiting, epigastric distress, and rarely dizziness. Overdosage may result in CNS depression (drowsiness and lightheadedness) or CNS stimulation and salicylate intoxication (requires induced vomiting or gastric lavage, specific parenteral electrolyte therapy for ketoacidosis and dehydration, and observation for hypoprothrombinemic hemorrhage [usually requires whole blood transfusions]). Meprobamate may cause drowsiness, ataxia and rarely allergic or idiosyncratic reactions. These reactions, sometimes severe, can develop in patients receiving only 1 to 4 doses who have had no previous contact with meprobamate. Mild reactions are characterized by urticarial or erythematous maculopapular rash. Acute nonthrombocytopenic purpura with petechiae, ecchymoses, peripheral edema and fever have been reported. If allergic reaction occurs, meprobamate should be stopped and not reinstituted. Severe reactions, observed very rarely, include angio-neurotic edema, bronchial spasms, fever, fainting spells, hypotensive crises (1 fatal case), anaphylaxis, stomatitis and proctitis (1 case) and hyperthermia. Treat symptomatically such as with epinephrine, antihistamine and possibly hydrocortisone. A few cases of leucopenia, usually transient, have been reported following continuous use. Rarely, cases of aplastic anemia (1 fatal case), thrombocytopenic purpura, agranulocytosis, and hemolytic anemia have been reported; almost always, in the presence of known toxic agents.

Composition: 150 mg. meprobamate, 75 mg. ethoheptazine citrate and 250 mg. aspirin per tablet.

Wyeth Laboratories Philadelphia, Pa.

when bursitis hits a 280-lb. tackle, hit back with Butazolidin alka



Indications: Osteoarthritis, rheumatoid arthritis, rheumatoid spondylitis, psoriatic arthritis, acute gout, painful shoulder (peritendinitis, capsulitis, bursitis and acute arthritis of that joint), acute superficial thrombophlebitis.

Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently. Large doses of Butazolidin alka are contraindicated in glaucoma.

Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage occur. Make regular blood counts. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The most common are nausea, edema and drug rash. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ul-

For 280-lb. tackles — or 108-lb. housewives — Butazolidin alka can hasten recovery from the agonizing pain of shoulder bursitis.

It's not for every patient. Check carefully the Contraindications, Warning and Precautions shown below.

And adverse reactions may occur. The most common are nausea, edema and rash. Rarely, agranulocytosis has been reported. All adverse reactions are listed below, too.

Play-for-pay or workaday patients — when they come up with shoulder bursitis and your clinical judgment indicates Butazolidin alka — go with it.

And watch the comeback.



cer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately before or after meals or with milk to minimize gastric upset. Mild drug rashes frequently subside with reduction of dosage. However, rash accompanied by fever or other systemic reactions usually requires withholding medication. Purpuric rash has also been reported. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, or a generalized allergic reaction similar to serum sickness may occur and require permanent withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

6509-V(B)R2

Butazolidin[®] alka

Capsules

100 mg. phenylbutazone
100 mg. dried aluminum hydroxide gel
150 mg. magnesium trisilicate
1.25 mg. homatropine methylbromide

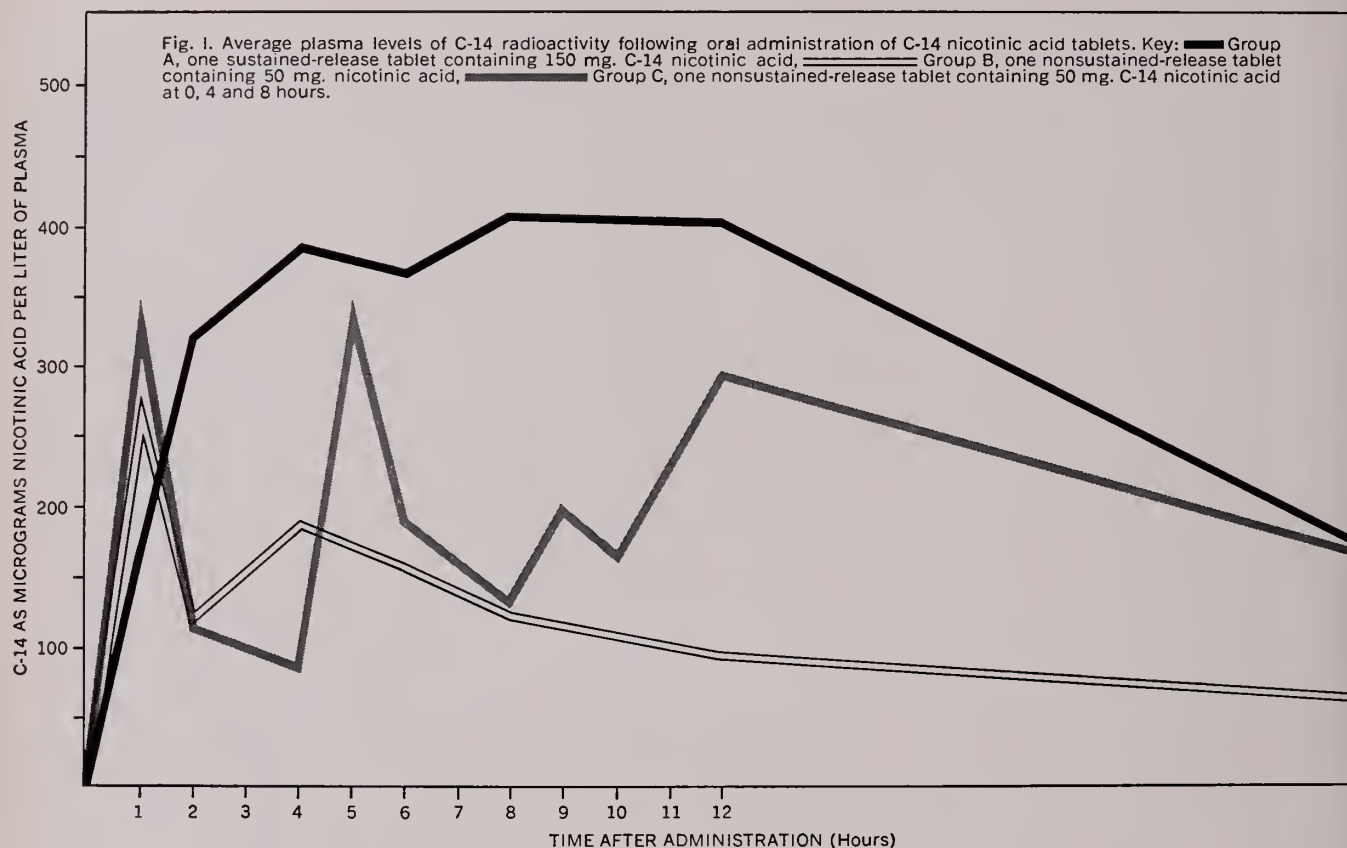
Dosage in painful shoulder: Initial: 3 to 6 capsules daily in 3 or 4 equal doses. Trial period: 1 week. Maintenance dosage should not exceed 4 capsules daily; response is often achieved with 1 or 2 capsules daily.

For complete details, please see full prescribing information.

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation, Ardsley, New York



Sustained circulatory, respiratory and cerebral stimulation for the



(fewer absent doses by
absent-minded patients)

Human volunteer subjects were administered Geroniazol TT tablets with the nicotinic acid component made radioactive with C-14. Plasma and urine samples were analyzed. (See Figures I and II) The radioactive tracer study substantiated the previous clinical evidence that the release of nicotinic acid from the Geroniazol TT tablet produced a gradual rise in plasma levels to a plateau for a total of 12 hours and more.

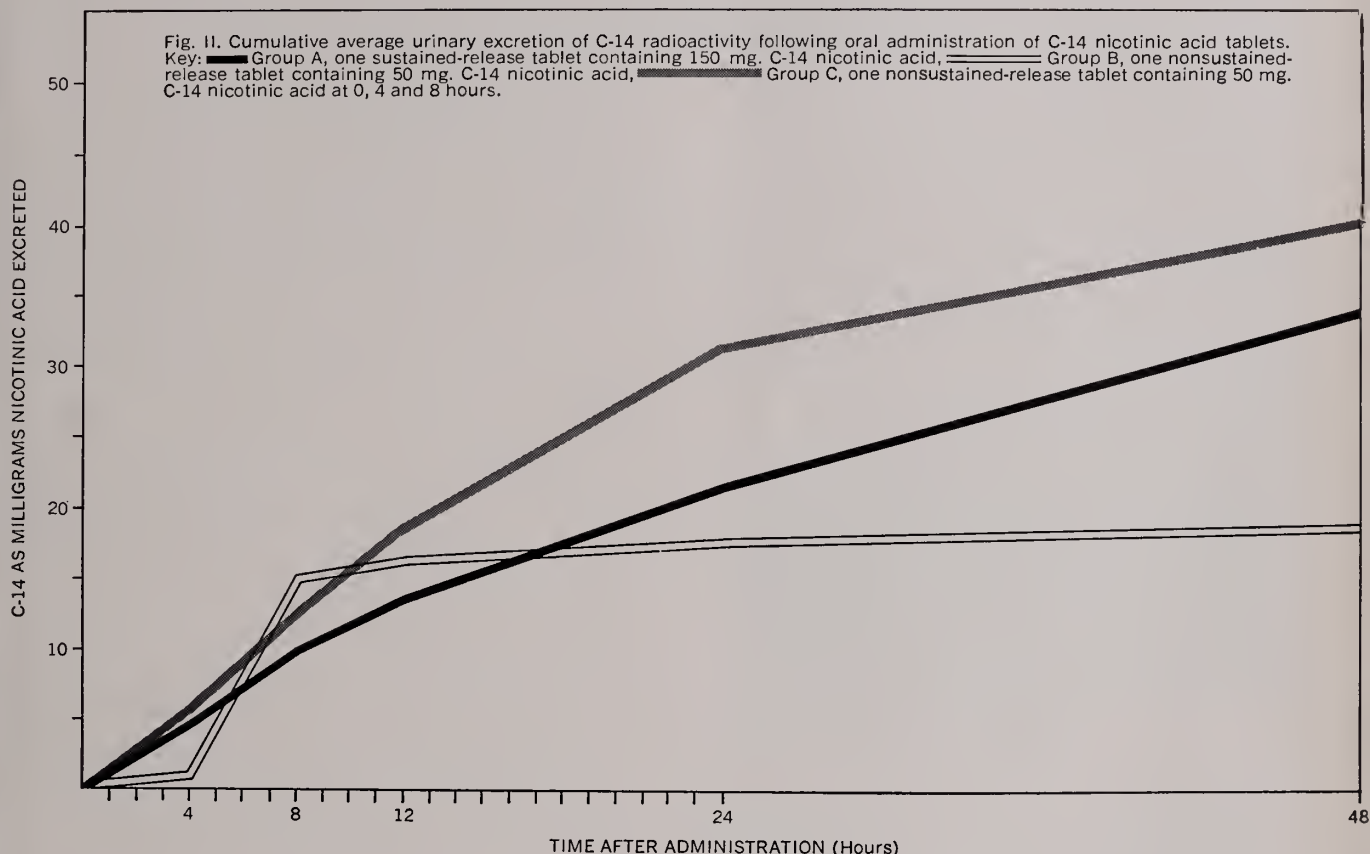
Such proven sustained activity makes the management of geriatric patients much easier by minimizing the possibility of neglected doses through absent-

mindedness or senile confusion. Therapy *can* be continuous on a daily dose of only one Geroniazol TT tablet every 12 hours.

The gradual release of nicotinic acid in Geroniazol TT will provide the well-known peripheral vasodilatation needed in patients with deficient circulation and with a minimum amount (if any) of "flushing." Also, cerebrovascular circulation is complemented by pentylenetetrazol, long-established as a cerebral and respiratory stimulant.

Geroniazol TT improves the typical, unfortunate, signs of senile confusion. Patients become more alert,

aged and debilitated



less confused and moody. Personal care, memory, emotional stability, social attention improve. Fatigue, apathy and irritability are reduced.

A prescription for 100 tablets of Geroniazol TT will permit your patients to enjoy the benefits of time-prolonged nicotinic acid/pentylenetetrazol therapy, at an economical price. Dosage is only one tablet every 12 hours.

Contraindications: There are no known contraindications.

Precautions: Exercise caution when treating patients with a low convulsive threshold.

Side Effects: Side effects are rarely encountered, however due to the vasodilatation effect of nicotinic acid, transitory mild nausea, flushing, tingling and pruritus are possible.

Dosage: One tablet every 12 hours.

Supplied: Prescribe bottles of 100 tablets, to take advantage of recent price reduction.

References: 1. Report by Nuclear Science & Engineering Corp., Pittsburgh, Pa., in files of Philips Roxane Laboratories. 2. Connolly, R.: W. Virginia Med. J. 56:263 (Aug.) 1960. 3. Curran, T R., and Phelps, D. K.: Am. Pract. & Digest Treat. 11:617 (July) 1960.



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nicotinic acid 150 mg., pentylenetetrazol 300 mg.
Tempotrol[®] Time Controlled Tablet



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■ **exceptional economy**—Due to its high neutralization capacity combined with low cost (about 1¢ or less per tablet), Dicarbosil is within the reach of all patients.

1. Schleif, R.H.: J.A.P.H.A., 46:179,1957 *U.S. Pat. No. 3,062,714

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Before prescribing, please consult complete product information, a summary of which follows:

Contraindications: Infants, patients with history of convulsive disorders, glaucoma or known hypersensitivity to drug.

Warning: Not of value in the treatment of psychotic patients, and should not be employed in lieu of appropriate treatment.

Precautions: Limit dosage to smallest effective amount in elderly or debilitated patients (not more than 1 mg, one or two times daily initially) to preclude ataxia or oversedation, increasing gradually as needed or tolerated. As is true of all CNS-acting drugs, until correct maintenance dosage is established, advise patients against possibly hazardous procedures requiring complete mental alertness or physical coordination. Driving during therapy not recommended. In general, concurrent use with other psychotropic agents is not recommended. If such combination therapy is used, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium (diazepam), such as phenothiazines, barbiturates, MAO inhibitors and other antidepressants. Advise patients against simultaneous ingestion of alcohol or other CNS depressants. Safe use in pregnancy not established. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Observe usual precautions in impaired renal or hepatic function. Periodic blood counts and liver function tests advisable in long-term use. Cease therapy gradually.

Side Effects: Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances, acute hyperexcited states, hallucinations); changes in EEG patterns during and after drug treatment. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms (convulsions, tremor, abdominal and muscle cramps, vomiting, sweating) similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.

Dosage—Adults: Mild to moderate psychoneurotic reactions, 2 to 5 mg b.i.d. or t.i.d.; severe psychoneurotic reactions, 5 to 10 mg t.i.d. or q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; muscle spasm with cerebral palsy or athetosis, 2 to 10 mg t.i.d. or q.i.d. *Geriatric patients:* 1 or 2 mg/day initially, increase gradually as needed and tolerated. (See Precautions)

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 50 and 500.



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Please see opposite page for important prescribing information.





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The Arthritis Foundation is the sole national voluntary health agency committed to conquering the rheumatic diseases. It provides the means for dynamic partnership between physicians and laymen to marshal leadership and resources toward the solution of this major national health problem.

The Arthritis Foundation looks forward to rapid growth with increasing opportunity for physicians to participate in the arthritis movement. For further information about The Arthritis Foundation and its programs write to the Foundation chapter in your community or to the Medical Department, Box 2525, New York, N.Y. 10001.

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Diagnosics

Medical Management of Muscular Dystrophy*

PROGRESSIVE MUSCULAR DYSTROPHY is a disease that causes muscle atrophy in young children, usually boys. If you have a muscular dystrophy patient, perhaps your diagnosis wasn't made until the child was three, four, or even seven years old—when his parents noticed an increasing clumsiness running or climbing stairs.

At first his little clumsiness was probably passed off: "Let your son develop according to his own growth. I have checked him, and find nothing wrong. You know, it takes a while for each child to develop his co-ordination and skill level—don't worry, every child is different."

But the parents do worry, and as the progressive weakness becomes more evident, so do you. The child's calves are hypertrophied, he walks on his toes, and to get up from a sitting position he 'climbs up his legs.' Serum enzyme analysis reveals elevated LDH, CPK, and aldolase levels. The diagnosis is made: Duchenne's progressive muscular dystrophy.

The course of the disease is well known. The atrophy advances from the musculature of the hips and shoulders to the extremities, and by early adulthood the child—with severe contractures and an inadequate vital chest capacity—is an invalid. He will die from a respiratory infection. A common cold will kill him.

You cannot cure the disease, but you can do many things to help the child and his parents.

A child with muscular dystrophy learns early that he is failing. He knows that yesterday he could climb the stairs—today he is having trouble. Repeated failure is as defeating to a child as it is to an adult. You know his need for accomplishment—to function on his own—to grow emotionally, mentally, and socially. The child must be somewhat independent.

But, do the parents understand this?

The tendency to over-protect their son is natural, but it will harm him emotionally and physically. You must help these parents expect and insist on capacity performance from the child, for anything less will hasten the disease process. Encourage them to provide love and understanding, not pity, and to respect the youth's desire for independence.

The child's wishes and needs for independence can be met with physical therapy that will maintain his mobility. Joint mobility, the most essential aspect of your treatment, can be preserved or restored with normal range of motion exercises—by moving the body parts through the normal full range possible.

These exercises, if done several times a day, can prevent contractures and deformity. Prescribed with breathing exercises, normal range of motion methods will help maintain vital lung capacity and lower the threat of respiratory infections.

Your patient can do many of these exercises himself, and by experiencing the thrill of achievement and approval, grow in self-respect and confidence.

However, the exercise routine must not be too strenuous. The therapeutic rationale is to keep the child working at his capacity, but not to overtax his resources. The exercises you prescribe and the result will of course depend on the child's condition. How vigorous a program you prescribe will be based on your own common sense and professional judgment, for if the child is over-protected, he will

*Supported in part by the Vocational Rehabilitation Administration Research and Training Grant 2, Department of Health, Education and Welfare, Washington, D. C.

Continued

'go down hill;' on the other hand, if he is overworked, he will also 'go down hill.' The key phrase is 'to his capacity.'

The sooner a daily routine of exercise is established, the more successful will be the treatment. The child will be happier and healthier. His whole body will function better—his circulation (ischemic ulcers will be decreased or eliminated), his digestion (including urinary tract functions) and his respiration.

If the child becomes ill, antibiotics are the treatment of choice, but bed rest must be forbidden unless absolutely necessary, as bed rest can hasten the progress of muscular dystrophy. Dr. Frederic Kottke at the University of Minnesota reports a three percent muscle strength loss per day of total inactivity for normal muscle.

In the last stages of the disease, lifting and nursing care can become a problem. The use of the exercise program and suitable braces will allow the child to remain at home. Orthopedic braces will also prevent the skeletal deformities and help the child maintain his mobility; but they may be shunned by the parents. Help the parents to emphasize their child's abilities, not his disabilities. As one doctor puts it, "Don't say he can't walk without braces—why not say he *can* walk—with braces?"

A Procedure for Range of Motion

General principles:

- Do not exceed your patient's existing range of motion.
- Do not use force.
- Keep all movements within a pain-free range.
- Do all movements smoothly and slowly.
- Do each movement three times during an exercise period.
- Do the exercises at least twice a day.

Head: (Figures 1, 2, and 3)

1. Bend head forward.
2. Bend head backward, keeping chin in.
3. Bend head toward left shoulder, then straighten. Bend head toward right shoulder, then straighten.
4. Turn face to left side, then face forward. Turn face to right side, then face forward.



Figure 1



Figure 2



Figure 3

MUSCULAR DYSTROPHY

Trunk : (Figure 4)

1. Bend body forward.
2. Bend body backward, keeping stomach muscles tight.
3. Bend body left, then straighten. Bend body right, then straighten.
4. Twist body left, then forward. Twist body right, then forward.



Figure 4

Shoulder : (Figure 5)

1. Raise arm forward and upward.
2. Raise arm sideways and upward.
3. Put palm of hand on back of neck, then bring hand down under arm, touching back of hand to shoulder blades.



Figure 5

Elbow :

Bend arm until finger tips touch shoulder, then straighten arm.

Forearm :

With elbow bent at a right angle, with palm down—turn palm up, next turn palm down.

Wrist :

1. Move hand forward, then move hand backward.
2. Move hand toward thumb, then toward little finger.

Fingers and thumb :

1. Bring tips of fingers to palm of hand, then straighten fingers.
2. Spread fingers wide apart keeping fingers straight, then bring fingers together.

Continued

DIAGNOSTICS

3. Keeping fingers straight, bend hand at knuckles.
4. Bend thumb to center of palm, keeping thumb close to hand, then straighten thumb.
5. Place thumb in front of forefinger, bring thumb straight out, then bring thumb back to forefinger.
6. Touch tip of thumb to tip of little finger, open hand wide; do this with each finger.

Hip: (Figure 6)

1. Bend hip with flexed knee.
2. Move leg backward as far as possible, keeping knee straight, then return it to starting position.
3. Move leg out to side as far as possible, keeping knee straight and toes pointed straight ahead; return it to starting position.
4. Sitting with lower part of leg hanging down, move one foot inward across other leg, rotating thigh outward.
5. Sitting with lower part of leg hanging down, keeping knees together, move one foot away from other foot rotating thigh inward.

Knees: (Figure 6)

Bend knee as far as possible, straighten leg.



Figure 6

Ankle:

1. Bend foot up; bend foot down.
2. Turn foot in; turn foot out.
3. Turn foot in and up with toes bent down.

Toes:

1. Bend toes down.
2. Bend toes up.

Nancy Sutton*
Minneapolis, Minnesota

*Assistant Scientist, Department of Physical Medicine, University of Minnesota Hospitals.
Photo Credit: J. Jones, Department of Physical Medicine and Rehabilitation, University of Minnesota.

DERIVATIVELY SPEAKING

Lung—from Anglo Saxon *lungen* (light in weight)

Scars

God will not look you over for medals, degrees or diplomas, but for scars.

—Elbert Hubbard

Minnesota Medicine at a Glance

Enteropathogenic *Escherichia Coli* in Children—Needham and Wenzl

Page 1311

The occasional finding of enteropathogenic *Escherichia coli* in the stool culture of infants and children with diarrhea should not be considered diagnostic, for the proportion of healthy infants with these organisms is about the same as the proportion of sick infants with these organisms. No special treatment need be recommended for these sporadic cases. Nevertheless, epidemic infections, especially if they affect hospitalized infants, are of grave concern and many necessitate antibiotic treatment and other special precautions.

Bronchial Asthma—Rowe and Rowe

Page 1321

Rowe and Rowe, practicing in the Bay area of California, believe that food is the sole cause of respiratory manifestations of allergy, as discovered in their practice. Their article emphasizes the importance of the history in asthma. By treating the food allergy they have achieved good results in asthma patients, but no improvement in patients who have emphysema. They have found cereals to be particular offenders.

Hemostasis and Thrombosis—Quick

Page 1333

Doctor Armand J. Quick, discoverer of the prothrombin time and an international authority on coagulation, gives his views on clotting. He sees hemostasis as three phases—vascular, platelets, and coagulation. Of these, the vascular phase accounts for most bleeding problems; and of vascular phase defects, Minot-Von Willebrand syndrome is the most common. This syndrome, although usually mild, commonly causes nose bleeds, gastrointestinal hemorrhage, and menorrhagia. To diagnose it, Doctor Quick suggests physicians use the Duke bleeding time and the aspirin tolerance test. The latter test—or bleeding times before and after a given dose of aspirin—helps physicians to diagnose Minot-Von Willebrand syndrome in patients who bleed or who have subclinical disease.

Angiosarcoma of Lungs—Kern et al.

Page 1339

Two months after onset of hemoptysis, a 57-year-old man underwent lobectomy for possible bronchogenic carcinoma. Pathologic studies showed infarction but no signs of neoplasia. One month later, biopsy of the lung revealed atypical cellular proliferation that in some places suggested Kaposi's sarcoma. The patient died two months later. Autopsy disclosed tumor nodules throughout the lungs. The left adrenal was replaced by a large mass. The pulmonary nodules contained neoplastic cells apparently of endothelial origin. The adrenal mass was made up of neoplastic spindle-shaped cells.

This case represents a rare primary angiosarcoma of the adrenal with either metastatic or simultaneous multifocal pulmonary involvement.

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REACTIONS: Allergic phenomena such as polyarthropathy, fever, skin eruptions, and acute generalized morbilliform eruptions with or without fever. Rarely, dermatitis goes on to exfoliation with hepatitis, and further dosage is contraindicated. Gingival hypertrophy, hirsutism, and excessive motor activity are occasionally encountered. During initial treatment, side effects may include gastric distress, nausea, weight loss, nervousness, sleeplessness, feeling of unsteadiness. Macrocytosis, megaloblastic anemia, leukopenia, granulocytopenia, thrombocytopenia, pancytopenia, agranulocytosis, and aplastic anemia have been reported. Nystagmus, lymphadenopathy, lupus erythematosus, erythema multiforme (Stevens-Johnson syndrome), and a syndrome resembling infectious mononucleosis with jaundice have occurred. DILANTIN is supplied in several forms including Kapseals® containing 0.1 Gm. and 0.03 Gm. diphenylhydantoin sodium.

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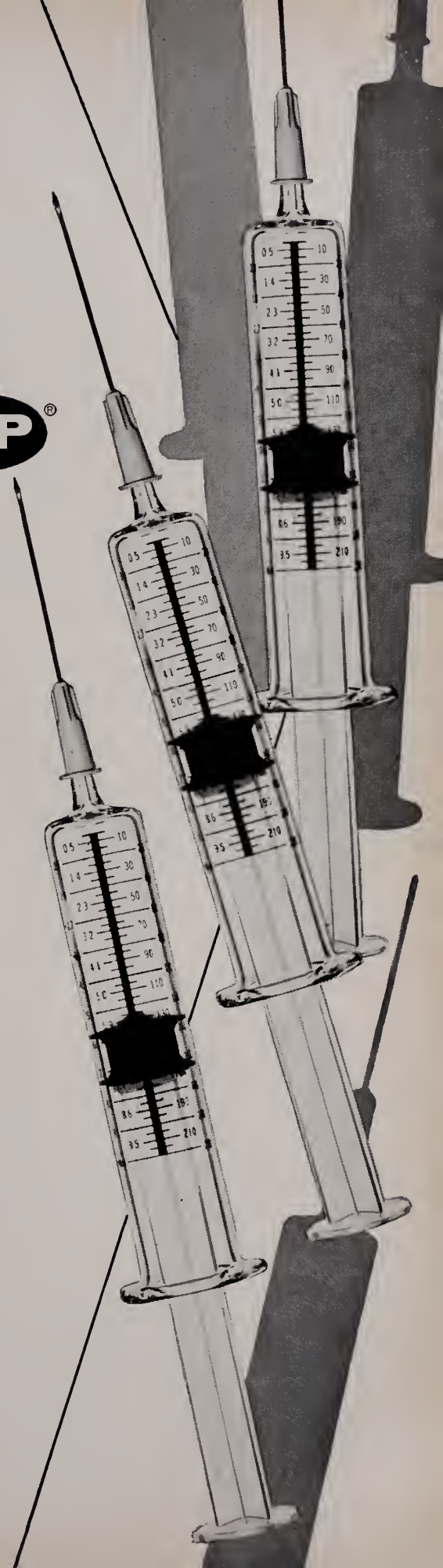
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References: 1. Batterman, R. C., and Grossman, A. J.: *Fed. Proc.* 14:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: *The Pharmacological Basis of Therapeutics*, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Roth, J. L. A., et al.: *Gastroenterology* 44:146, 1963. 4. Conney, A. H., and Burns, J. J.: *J. Pharmacol. Exp. Ther.* 129:340, 1960. 5. Settel, E.: *Clin. Med.* 6:1373, 1959. 6. Berman, H. H., et al.: *Dis. Nerv. Syst.* 25:430, 1964. 7. Darienzo, C.: *Ibid.*, 27:189, 1966.

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President's Letter

READ NO further unless you want to hear a small story about one of my own personal experiences, which I thought I would like to pass on to you for what it may be worth.

If you have never been a smoker, this may bore you!!!

If you have ever smoked and quit, we can compare notes!!!

This really is written for those of you who haven't quit smoking as yet and may be toying with the idea, but need a push.

For those of you who intend to continue polluting the atmosphere and yourselves, my story may amuse you, and you can smile cynically to yourselves and call the whole thing quite stupid.

The incident which gave me the idea to write this little piece was that I happened to tell my story to a Ph.D. clinical psychologist friend of mine, with whom I work at the St. Peter State Hospital. I thought no more about it until I discovered that he had switched to cigars after being a heavy cigarette smoker. He informed me that he had given my tale some thought and had been so impressed by it that it is now his intention to quit smoking altogether. I figured it this way. If my story could affect him so much, a *clinical psychologist*, mind you, and a Ph.D., to boot, then it just *might* give some of you an idea to do the same.

There is nothing worse than a reformed rakehell. One becomes a missionary of sorts,

and tries to make his revelation appealing to all he meets!! So pull up a chair, while I spin my tale of sanctification!

It all started in the winter of 1953: the year that the Kent cigarette was introduced. I had attended a medical meeting in St. Louis, where a battery of automatic smokers had been pulling smoke from a dozen brands through filter papers. Lo and behold—there was almost nothing to be seen on the filter paper which came from the Kent brand! Obviously, they were not advertising Camels! At that time I used a filter in a holder, so I put a Kent on the end of that, and what got back to me was a big fat zero as far as taste was concerned. This gave me the idea: a Kent cigarette would be the one to use when I decided to quit. I bought a carton, smoked them up, and haven't touched cigarettes since!!

I began this whole project by telling myself about all the ways that my lousy habit created discomfort for others. I had to admit it. I stunk! Every smoker does, especially to a nonsmoker. If I went visiting and stayed very long, *I had to have a smoke*. Did they mind? Of course not! What else could they say? No one in the home smoked, so there were no ashtrays about, but they would get something for me. Thanks! That's a lovely old China dish! And smoke clings to curtains and clothing for days!

OOPS! So sorry about that hole in your

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minnesota medicine

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|| Porphyria

Strange

and

Baffling

Ailment

HARRY W. SHUMAN, M.D., F.A.C.P.
Rock Island, Illinois

W. D. SNIVELY, JR., M.D., F.A.C.P.
Evansville, Indiana

AMONG THE MOST bizarre and weird of ailments is porphyria, a disorder of blood pigment metabolism in which porphyrins are produced in excess. The disease presents a trio of paradoxes: although porphyria is inherited, acute attacks can be precipitated by chemicals; although physical symptoms such as abdominal pain, vomiting and constipation are preeminent, mental disturbances, ranging from emotional instability to psychosis, almost always accompany them; the very therapy which physicians might quite naturally use to treat the mental disturbances actually accentuates the severity of the disturbances.

The disease has played a fascinating role in history, probably causing the alleged insanity of King George III, and possibly the death by burning at the stake of sufferers from porphyria, adjudged werewolves. Of immediate importance, porphyria is not extremely rare. At least 203 cases have been reported; many more have no doubt gone unreported. Every physician should, therefore, be familiar with this strange ailment.

The Nature of Porphyria

An anomaly in pigment metabolism, porphyria represents a group of disorders of porphyrin metabolism or disturbances of pyrrole* biosynthesis. It is usually inherited. Relatively large amounts of uroporphyrins appear in the urine. Usually excretion of coproporphyrins is increased. In some forms of the disease, excretion of porphyrin precursors (delta-aminolevulinic acid and porphobilinogen) is increased.

Based on clinical and biochemical distinctions, one can divide porphyria into two major groups:

Erythropoietic Porphyria

This rare form of porphyria is inherited in either sex as a mendelian recessive trait. It re-

*See Test Your Word Score Page 1513.

sults from abnormal heme biosynthesis that leads to overproduction of porphyrins of Type 1 isomer. A defect in the enzyme system of the normoblast causes production of increased quantities of Type 1 uroporphyrin. Deposits of uroporphyrin 1 into the skin apparently cause photosensitivity.

Skin lesions, such as a bullous-vesicular dermatitis (hydraea aestivale) occur on exposed surfaces. Hypertrichosis*, melanosis and increased susceptibility of the skin to trauma are seen, as are hemolytic anemia and splenomegaly. Teeth may turn red. Bones may appear red at postmortem. The urine is pink or red and contains large quantities of uroporphyrin 1 and coproporphyrin 1.

Treatment includes avoidance of sun exposure, protective ointments, anti-inflammatory ointments and, in some instances, splenectomy.

Hepatic Porphyria

a. Acute Intermittent Porphyria

This variant of porphyria is believed inherited as a mendelian dominant trait. It is caused by overproduction of the porphyrin precursors, delta-aminolevulinic acid and porphobilinogen, resulting from disturbances of pyrrole biosynthesis. Porphobilinogen and porphyrins accumulate in the liver. Affected persons may have no symptoms or may show clinical manifestations of varying severity. The disease may be without symptoms for long periods, with acute intermittent attacks.

The most common manifestations are paroxysms of abdominal pain, usually colicky and associated with vomiting, distention, and diarrhea or constipation. Colic can mimic a number of acute abdominal conditions. It is usually accompanied by leukocytosis and gastrointestinal spasm. Various neurologic disturbances may occur suddenly—so may convulsive seizures. Most patients develop psychiatric manifestations ranging from irritability to major psychoses. *Photosensitivity does not occur nor do cutaneous lesions.*

Although the urine usually is colorless, it may become wine-colored or black when exposed to sunlight. It contains large quantities of porphobilinogen, usually with increased

amounts of delta-aminolevulinic acid and of uroporphyrins and coproporphyrins. Porphyrins can be studied through their properties of fluorescence with chromatographic methods, melting point of methyl esters, and characteristic spectral absorption bands. Family studies are indicated when an active case is encountered.

Therapeutic measures include chlorpromazine, electrolyte replacement therapy, adrenal steroids, and adenosine monophosphate.

Barbiturates, infections, alcohol and toxic agents such as lead may produce attacks. Use of analgesics and sedatives should be minimized.

b. Photosensitive Hepatic Porphyria (*porphyria cutanea tarda*)

• Hereditary Form

This form of the disease usually develops after age 20. Apparently it is a disturbance of hepatic catalase metabolism associated with accumulation of uroporphyrins in the liver. They are also deposited in the skin, causing photosensitivity. There is continuous excretion of large amounts of coproporphyrin in the feces during latent and active periods. During the active periods, the urine contains large amounts of porphobilinogen and delta-aminolevulinic acid, plus uroporphyrins and coproporphyrins.

• Symptomatic Form

This form may be acquired. Impaired liver function underlies it. However, additional factors may be responsible, such as hepatoma, exposure to certain industrial chemicals, lead intoxication, ingestion of flour grown from seed wheat in contact with hexachlorobenzene, and alcoholic or nutritional cirrhosis. The urine contains a marked increase of uroporphyrins and coproporphyrins, but normal amounts of porphobilinogen and delta-aminolevulinic acid.

Treatment includes protection from the sun's rays; high protein diet; avoidance of alcohol, barbiturates and sulfonamides. Chlorpromazine may be useful.

c. Mixed Porphyria

Combined intermittent and photosensitive hepatic porphyria includes the rare cases in which paroxysms of abdominal pain and neurologic manifestations combine with photosen-

*See Test Your Word Score Page 1513.

sitivity. This form is hereditary. The urine shows a normal or a red color and contains large amounts of uroporphyrins and coproporphyrins.

A Nightmare Disease

Over the centuries, porphyria has made life



Fig. 1—King George III

a living nightmare for its victims and a diagnostic nightmare for physicians. Illis, of Guy's Hospital, London, has called attention to the striking similarity between the several manifestations of porphyria and the descriptions in older literature of werewolves. He believes that the red teeth, the passage of red urine, the nocturnal wanderings, the facial lesions with flaring, wolf-like nostrils, the mutilation of the hands, could well have suggested transformation into a werewolf in primitive, fear-ridden communities.

Much closer to the present is the case of King George III, of England. Although most of us were not presented with a picture complimentary to this monarch in our school days, since he was responsible, in part, at least, for the American Revolution, he was in retrospect one of England's more competent, dedicated rulers, until he had his first attack of what Macalpine and Hunter believe to have been a classic case of porphyria.

Certainly the classic picture of the illness of George III, beginning about the year 1767, appears to meet the criteria for porphyria. The king had his first major attack in 1765, at the age of 26 or 27. He was to have at least five major and four minor attacks before he died January 29, 1820, in his 82nd year, blind, deaf, and generally miserable. Most of his attacks started in winter, and each attack left him increasingly wasted and weak. In addition to manifesting almost all of the clinical findings of porphyria, he was said to have passed "bloody water" during one period of 16 hours, and water of a deep color, leaving a pale blue ring upon the collecting vessel, on another.

All in all, the king's illness was a long and sorrowful one in which he suffered "severely from his affliction, pitifully from his treatments, and miserably from his management . . ." One of his physicians, Dr. Francis Willis, who boasted that he broke in patients as he did horses, ordered the king clapped in a "winding sheet," or a restraint chair (the king bitterly dubbed this his "coronation chair"), or in a strait waistcoat with his legs tied to the bed. Of sound mentality, at least during his early years, he said pathetically in 1801: "I do feel myself very ill, I am much weaker than I was, and I have prayed to God all night that I

might die, or that He would spare my reason . . . should it be otherwise, for God's sake keep me from your father [Dr. Francis Willis]."

Since acute intermittent porphyria is a familial disease, relatives can be expected to develop it. The younger sister of King George III, Caroline Matilda, died at the age of 24 from an illness said to be completely compatible with a fulminating attack of acute intermittent porphyria. Since George III was a member of the House of Hanover, research into the medical histories of the numerous members of his family—many of whom lived abroad—might prove most illuminating.

Case Report

In the case here reported, acute intermittent porphyria was associated with myocardial infarction. An attack was precipitated by the administration of barbiturates before the diagnosis was made. The combination of two major ailments offered a perplexing diagnostic problem. Myocardial infarction associated with acute intermittent porphyria occurs infrequently. The syndrome should be suspected when the characteristic radiating arm pain of myocardial infarction is accompanied by generalized abdominal pain and psychologic abnormalities.

History

A 55-year-old white male, who farmed and operated an automobile crane for a livelihood, first noticed intermittent bilateral arm pain early in January, 1963. On January 30, he awakened in the early morning with intensified arm pain accompanied by what he described as a "strangling feeling in the back of the head." His arms felt "as though they were breaking off." On the morning of the following day he consulted his family physician. A chest x-ray revealed no abnormalities; an electrocardiogram was interpreted as indicating myocardial ischemia. The patient continued working until February 14, 1963, when the senior author saw him.

The past history revealed that the patient had experienced mild intermittent pain in the arms and shoulders for the previous one or two years, not always associated with exertion. Also about two years previously, the patient had passed some dark-colored urine believed at the time to be bloody. There was no pain or urinary tract symptoms at the time, nor was there a repetition of the episode.

The patient's wife, with diabetes, was 55. A son, aged 32, was in good health. The father died at the age of 51 as a result of an accident, the mother at the age of 47 because of "heart trouble with dropsy." The patient had three brothers, aged 72, 68 and 57, in good health.

Physical Examination

The patient was physically well developed; pulse rate 80 and regular, blood pressure 150/80, respirations 24 per minute, oral temperature 99.8F., weight 68 kg. and height 167 cm. He was well oriented and did not appear ill. His voice was high-pitched, and he was apprehensive. The skin of his face was more pigmented than the rest of the body; however, there were no areas of depigmentation elsewhere. Telangiectatic arterioles were prominent over both cheeks and the bridge of the nose. There were several artificial teeth in the upper jaw. The tongue was coated and brownish in color. Otherwise the head and neck were normal.

The anteroposterior diameter of the chest was within normal limits. Expiration was slightly prolonged with scattered rales in each lung base. No cardiac abnormalities were discovered. The liver edge was not felt, nor could the spleen be palpated. The

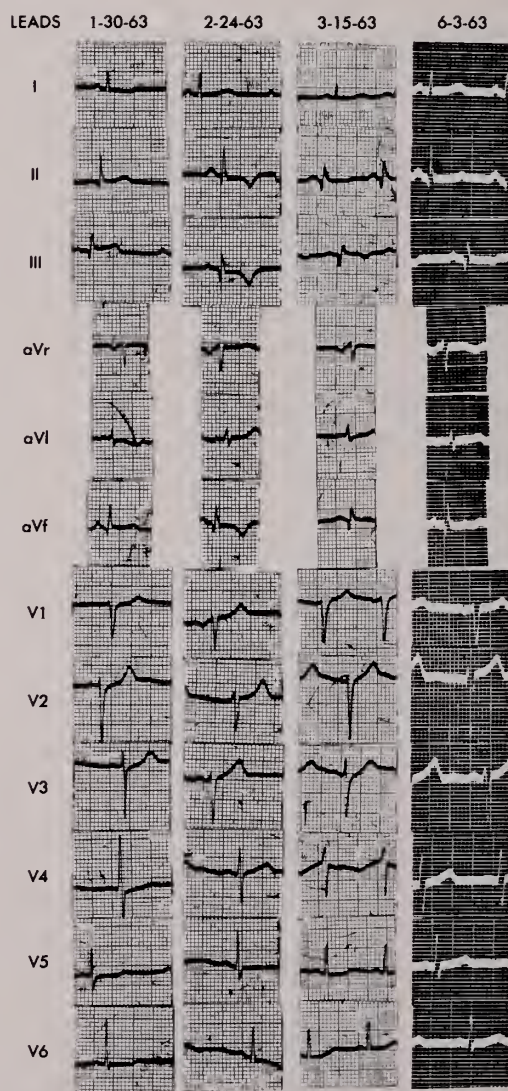


Fig. 2—Serial tracings of acute posterior myocardial infarction with healing and stabilization.

prostate was of average size, smooth and regular. Rectal examination was negative.

Neurological examination revealed hyperactive deep tendon reflexes in both arms. No abnormalities of the cranial nerves were detected. Tremors of both hands and marked adiadosokinesis* of both wrists were present. The abdominal reflexes were diminished and the cremasteric reflexes hyperactive. Deep tendon reflexes were absent at the knees, although the ankle jerks were increased. There was unsustained bilateral ankle clonus. When the patient stood, he had a vacant, staring expression and either ignored questions or responded slowly to them.

Progress

Since the patient refused to remain in bed and was restless and agitated and complained of aching in the arms as well as severe abdominal distress, he was hospitalized on February 17. Because of his restlessness, barbiturates were started. Severe intermittent arm pain associated with diffuse abdominal cramps and backache continued. The abdominal pain was most distressing to the patient and was accompanied by intractable constipation which failed to respond to laxatives and for which the patient continually requested enemas. On several occasions he sat in a bathtub of warm water to obtain relief. Following this therapy, he lay across the bed on his abdomen.

An x-ray of the lower bowel was done because of the obstinate motor inactivity and reported "... a gaseous distention of the intestine involving some of the small intestine, as well as the large bowel, as far as the region of the splenic flexure. Multiple fluid levels are present. The pattern at this time suggests the presence of a large bowel obstruction."

A follow-up barium study revealed that "the colon is filled from rectum to the caecum and no lesion is found. Evacuation is incomplete. Impression, normal colon; previous distention of March 10th has subsided." An electrocardiogram done on March 18 revealed evidence of Q waves in Lead₂ and Lead₃ with a characteristic posterior wall infarction pattern.

The dose of barbiturates was increased to lessen the patient's discomfort and abnormal mental state; the total amount of sodium pentobarbital administered was 4.7 grams. Although he had not used alcohol before, he managed to obtain a quart of wine which he drank secretly from time to time. At his own insistence, he was returned home.

Laboratory Data

After 24 hours the patient's wife insisted that he be readmitted to the hospital, where his behavior was characterized by increased agitation and his backache was so severe he could not lie down. He was extremely irritable, had a staring fixed expression, and was stuporous with catatonic manifestations. His wife noticed that his urine was dark; examination now revealed porphyrins. The 24-hour urine specimen obtained on March 27 was strongly positive for porphobilinogen, uroporphyrin and coproporphyrin. It was strongly fluorescent through ultraviolet light. The quantitative analysis revealed coproporphyrin 201 μ g/100 cc.; uroporphyrin 189 μ g/100 cc. The porphobilinogen was 3.2 μ g/100 cc.; estimated as 50 mg. per day, assuming a 1500 cc. output.

The delta-aminolevulinic acid was 2.6 mg. per cc.

The hemoglobin was 17.5 gm/100 cc.; red cells 5,750,000, and white blood cells 14,920 with segmented cells 67%; lymphocytes 32%, eosinophils 1%; hematocrit 51%, sedimentation rate (Wintrobe) 5 mm. per hour. The lactic dehydrogenase was 370 units (normal range 100 to 300 units). Total cholesterol was 230 mg. %; Kahn reaction negative; cephalin flocculations for 24 to 48 hours were negative; bilirubin 1 minute was 0 mgm; 30 minutes 0.8 mgm. The urine, normal on first admission, was strongly positive for porphyrins on the second.

On March 29, the cephalin flocculation for 24 hours was negative; for 48 hours it was 1-plus. The transaminase was 62 units; the bilirubin 1 minute 0.1 mgm. %; 30 minutes 0.5 mgm. %. The total protein was 5.4 Gm. %; total cholesterol 196 mgm. %. The alkaline phosphatase was 3.3 B.U. units; the thymol turbidity 1 unit; blood urea nitrogen 15.5 mgm. %. The sedimentation was 23 mm. per hour. The electrocardiogram revealed acute posterior myocardial infarction with healing and stabilization (Figure 2).

Additional liver function studies disclosed a thymol turbidity of 1.5 units; bromsulphthalein excretion 11.7%; transaminase 20 units. The cephalin flocculation was negative for 24-hour and 48-hour specimens. The urine was negative to the Watson-Schwartz test.

With the establishment of the diagnosis of porphyria, barbiturates, ordered on first admission to the hospital and continued since, were discontinued. Slowly the patient's mental symptoms disappeared. He became pleasant and cooperative and was discharged April 17, 1963. Follow-up electrocardiogram on November 25 revealed a stabilized, healed infarct with Q₂ and Q₃ residuals. Later tracings were normal except for the residual findings.

Discussion

The severe arm pain experienced by this patient probably stemmed from the myocardial infarction, aggravated by the neuropathy which accompanies porphyria. The neurologic manifestations of peripheral neuritis associated with porphyria are attributed to focal degeneration of axis cylinders, demyelination and Schwann cell proliferation.

Relatively few electrophoretic data on porphyria are available. Examinations of this patient's serum showed slight variations in the

TABLE I
ELECTROPHORETIC PATTERN*

Component	% Total Protein
Gamma 2 Globulin	10.9
Gamma 1 Globulin	2.7
Beta Globulin	7.5
Alpha 2 Globulin	12.0
Albumins	61.0
Pre Albumins	2.2
A/G Ratio	1.56
Total Protein	6.7
Sia Test	negative

*Moving boundary electrophoretic studies at pH 8.6 in 0.1 ionic strength diethyl barbiturate buffer.

*See Test Your Word Score Page 1513.

protein components (Table 1). The albumin and gamma globulins were normal. There were slight variations in the beta and alpha 2 globulins, probably not significant. The prealbumins were elevated. The serum iron level was high normal, while the unsaturated iron binding capacity was almost twice normal (Table 2).

TABLE 2

Electrophoretic iron studies serum
iron level 160 ug%.
Unsaturated iron binding capacity 384 ug%.

The crampy abdominal pain and constipation seen with porphyria have not been satisfactorily explained. Attempts to reproduce the symptoms in experimental animals have not been convincing. As the nomenclature for the ailment implies, the presence of reddish or wine-colored urine may be intermittent.

When diffuse, nondescript severe abdominal pain, psychic abnormalities and neuropathy of unknown origin occur together, either as a primary condition or in association with some other clinical syndrome, a Watson-Schwartz test should be done for the presence of porpho-

bilinogen.

Summary

Porphyria, a bizarre and weird disease with a fascinating history, still occurs. The practicing physician should, therefore, be aware of its protean manifestations. He should consider the possibility of porphyria whenever he sees a patient with abdominal pain, vomiting, constipation, muscular pain, tachycardia and psychologic disturbances—or various combinations of these—particularly when the urine is colored.

Patients diagnosed as having porphyria, and their relatives as well, should beware of barbiturates, sulfonamides, alcohol and various other chemicals. The case here reported combines a classic instance of porphyria with myocardial infarction.

Acknowledgment

The authors wish to express their deep appreciation to Doctor C. J. Watson, Professor of Medicine, University of Minnesota, for his kindness in performing quantitative measurements of the porphyrin components and interpreting the results, and to Doctor H. F. Deutch, Professor of Chemistry, University of Wisconsin, for the electrophoretic analysis.

References

- Schmid, R.; Schwartz, S., and Watson, C. J.: Porphyria Content of Bone Marrow and Liver in Various Forms of Porphyria. *Arch Intern Med* 93:167, 1954.
- Watson, C. J.: Porphyria, pp. 589-595, in Cecil & Loeb: *A Textbook of Medicine*, 10th ed, Philadelphia, Saunders, 1959.
- Fayez, M.: Acute Abdominal Porphyria. *J. Egypt Med Ass* 43:415, 1960.
- Waldenstrom, J., and Haeger, B.: The Liver in Porphyria Cutanea Tarda. *Ann Intern Med.* 53: 286, 1960.
- Dean, G.: Routine Testing for Porphyria Variegata. *S African Med J* 34:745, 1960.
- Tuffanelli, D. L.: Porphyria Cutanea Tarda Associated With Hemochromatosis. *U. S. Armed Forces Med J* 11:1210, 1960.
- Norris, W., and MacNab, G. W.: Anaesthesia in Porphyria. *Brit J Anaesth* 32:505, 1960.
- Cases From the Medical Grand Rounds, Massachusetts General Hospital, Case 478: Porphyria. *Amer Pract Dig Treat* 11:883, 1960.
- Malcoly, D. A.; Hightower, N. C., Jr.; Ibarra, J. D., Jr., and Haines, R. D.: Acute Intermittent Porphyria. *Texas J Med* 56:801, 1960.
- Sharvill, D.: Porphyria Cutanea Tarda. *Proc Roy Soc Med* 53:964, 1960.
- Okano, K.; Matsumoto, K.; Esumi, K.; Saki, T., and Kodama, J.: Three Cases of Acute Porphyria. *Acta Path Jap* 10:491, 1960.
- Bothwell, T. H.; Kramer, S.; Jacobs, P., and Barnes, H. D.: Iron Kinetics During Acute Episodes of South African Porphyria. *S African Med Sci* 25:141, 1960.
- Watson, C. J.: The Problem of Porphyria—Some Facts and Questions. *New Engl J Med* 263:1205, 1960.
- Eales, L.: The Porphyrins and the Porphyrins. *Ann Rev Med* 12:251, 1961.
- Kelenyi, G.; Illes, T., and Nemeth-Csoka, M.: Acute Intermittent Porphyria: Clinical, Laboratory and Autopsy Findings. *Acta Med Acad Sci Hung* 17:151, 1961.
- Moroni, P.: On the Possibility of Quantitative Interpretation of Paper Electrophoresis of Porphyrins. Investigations Made in 2 Cases of Porphyria Cutanea Tarda. *Arch Ital Derm Vener* 31:100, 1961.
- Peters, H. A.: Porphyric Psychosis and Chelation Therapy, Recent Advances. *Biol Psychiat* 4:204, 1961.

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Dogma

*Dogma does not mean the absence of thought, but the end of thought.—Ches-
terton*

Paradox of Brucellosis

Decreased
Incidence
but
Increased
Difficulty
in
Clinical
Recognition

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IN RECENT YEARS the incidence of brucellosis has considerably decreased in the United States. Paradoxically, for those with a special interest in the disease, diagnosis has become more difficult.

Contributing to this paradox is the fact that the more classic types of the disease are now recognized with relative ease, and management of such cases is generally satisfactory. Consequently, only atypical cases are likely to come under the scrutiny of physicians with a special interest in brucellosis. Some of these atypical cases involve a previous episode of acute brucellosis in which either the disease was unrecognized or less than optimal therapy was given. Such patients present with localized infection, and diagnosis often is comparatively more difficult. Also, among these patients there have been recognized new syndromes of this old disease, such as localized brucellosis of the spleen associated with recurrent constitutional manifestations.¹

Because of these considerations, it appears pertinent to review some of the currently applicable diagnostic and therapeutic facets of brucellosis. Continued interest in the disease by members of our group is attested by previous publications.¹⁻⁹

Some Nosologic Considerations

Members of our group continue to find it convenient to classify brucellosis as (1) bacteremic, (2) serologic, (3) localized, and (4) mixed.

Patients with bacteremic brucellosis generally are acutely and severely ill. In this type the essence of diagnosis is the culturing of brucellar organisms from the blood; serum agglutination titers usually are high and frequently are rising. Currently, this type of brucellosis is rarely encountered at the Mayo Clinic.

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Patients with the serologic type have acute or subacute systemic manifestations compatible with the disease, but cultures of the blood are negative for brucellar organisms. The essential characteristic in this type is detection of high, and preferably rising, serum agglutination titers. In the past, some workers have referred to this type as acute nonbacteremic brucellosis. Like the bacteremic type, this type of the disease is rarely encountered in our current practice.

Patients with the localized type sometimes are relatively asymptomatic, but the process may produce recurrent systemic manifestations. In our experience, such recurrent systemic manifestations are most commonly associated with localized splenic brucellosis. In localized pulmonary infections, lack of symptoms is common and detection of the lesion on routine roentgenograms of the chest is usual. Less frequently, other sites of brucellar localization, such as the liver and kidneys, may be asymptomatic, or relatively so. In contradistinction to the serologic or the bacteremic type, the process is chronic and the essential diagnostic finding is growth of *Brucella* on culture of the involved tissue.⁹ Agglutination titers as a rule are low or absent in this type, and results of blood cultures are negative; therefore, one's clinical suspicion must be correspondingly heightened if the diagnosis is to be made. In past years at the Mayo Clinic, the combined incidence of the bacteremic and serologic types was about four times that of the localized type; currently, at least, the converse is true.

The mixed type of brucellosis is very rare and is in an indeterminate area among the preceding types. A patient with bacteremic brucellosis and coexistent culturally proved brucellar spondylitis is an example.⁵

Some Clinical Manifestations

In either the bacteremic or the serologic type, such findings as fever, chills, and sweats of acute onset in a patient who has had possible contact with brucellar organisms usually imply consideration of the presence of the disease. In this regard, more than half of the patients studied by members of our group have been farmers or persons otherwise occupied with animal husbandry. Only about 10 per

cent of our patients with brucellosis have been females. In the bacteremic and serologic types of infection, splenomegaly is the most frequent abnormality and occurs in about 25 per cent of patients. In our experience, adenopathy and hepatomegaly each occurs in about 10 per cent of these types.

In contradistinction to the bacteremic and serologic types wherein about 90 per cent of the patients have fever, fever has been noted in less than half of our patients with localized brucellosis. There are some indications that the spleen may be the most common extraskeletal site of localized brucellosis in man. From 1952 through 1964, 10 patients with localized splenic brucellosis have been seen at the Mayo Clinic.⁸ Of the sites of brucellar localization, the following five (in order of decreasing frequency) have been most common in our experience: skeleton, spleen, genitourinary tract, soft tissues, and lungs.

The Spleen and Other Loci

In addition to the spleen, sites of chronic localized brucellar infection associated with recurrent constitutional manifestations are the liver, gallbladder, skeleton, lymph nodes, and ovarian cysts. The symptomatic episodes usually occur several times a year, and 10 years or more may pass before the process is identified. Lasting two to seven days, the episodes may be characterized by chills, fever, sweats, malaise, myalgia, and headache. Other symptoms related to the site of localization may be noted.

When present in localized brucellosis, physical findings are usually indicative of the site of involvement. For example, an enlarged spleen may be palpated in localized brucellosis of the spleen, or swelling and tenderness of a knee may manifest brucellar prepatellar bursitis. Before operation, the surgeon may be unaware of the nature of other localized lesions, notably those of the lungs, and his securing of material for culture may be of extreme value.

The Skeleton

Brucellar spondylitis in which the causative organisms invade an intervertebral disk from a nidus in the vertebral body is the most fre-

quent type of skeletal involvement.⁵ Whenever the so-called disk syndrome is seen in a patient who works with animals, the possibility of brucellar spondylitis should be considered. Back and leg pain, muscle spasm, percussion tenderness, and sometimes even a positive result to the Lasègue test may be noted. In our experience, brucellar spondylitis accounts for almost 50 per cent of the cases of skeletal brucellosis. However, brucellosis rarely involves the cervical spinal column. Osteomyelitis, which constitutes about 15 per cent of the cases of skeletal brucellosis, may involve such regions as the humerus, femur, skull, and ribs and may be manifested by local pain, heat, tenderness, swelling, erythema, and sometimes a variable degree of constitutional reaction. Although brucellar prepatellar bursitis is the lesion in roughly 25 per cent of the cases, brucellar synovitis occurs in only about 10 per cent. Since our report⁵ in 1960 on 36 patients with skeletal brucellosis, we have seen an additional four patients with culturally proved brucellosis of this variety. These patients had lumbar spondylitis, osteomyelitis of the pelvis, and infection of the synovial tissue of the knee and shoulder joint.

Urinary Tract or Liver

Brucellar involvement of the urinary tract may occur without physical manifestations and frequently cannot be differentiated from chronic infections of the urinary tract due to other pathogens, without definitive microbiologic findings.

Localized hepatic lesions caused by brucellar organisms may be asymptomatic or may result in hepatomegaly, jaundice, and constitutional reaction. Jaundice and altered hepatic function also are not uncommon in acute brucellar infection.

Lymphatic and Vascular Lesions

Chronic brucellar infection of a superficial lymph node may result in a draining sinus.

Although rarely causing vascular lesions, brucellar organisms have been cultured from a popliteal aneurysm removed at operation, and cases of brucellar endocarditis have been described.

*See Test Your Word Score Page 1513.

Laboratory Findings

Cultural

Brucellosis is diagnosed with certainty only by cultivation of brucellar organisms from specimens of the patient's blood, body fluids, excreta, or tissues. In bacteremic brucellosis, *Brucella abortus* is grown most frequently on cultures of the blood. In our experience, most localized lesions are caused by *B. suis*.

Serologic

As a generalization, in cases wherein brucellar organisms have not been cultured, the diagnosis of brucellosis should not be made unless brucellar agglutinins are present in high or increasing titer and the patient is strongly suspected clinically of having the infection. The agglutination test can lead to confusion in the form of the so-called anamnestic* phenomenon; in such an instance, the residual agglutination titer from previous brucellosis may be increased by the patient's current and unrelated disease. A previous injection of Brucellergin, a vaccination against cholera, or the presence of tularemia may also induce antibrucellar agglutinins. Our experience in regard to the agglutination test can perhaps be summarized as follows: In bacteremic brucellosis, titers invariably exceed 1:200 at some time during the illness, but in localized brucellosis, titers in more than half the cases do not exceed 1:200 and occasionally are negative. Brucellar spondylitis differs from other types of localized brucellosis in that the agglutination titer is almost always 1:800 or higher.

Hematologic

In most patients with brucellosis, routine hematologic data are of little diagnostic aid. The overall incidence of anemia in these patients is less than 10 per cent, but is more common in patients with the localized type than in those with the bacteremic or the serologic type. In patients with the bacteremic or the serologic type, leukopenia is present in about one third, but leukocytosis is rare. Leukopenia or leukocytosis is present in less than 10 per cent of patients with the localized type; rarely, leukopenia and thrombocytopenia occur as hypersplenic effects in localized splenic brucellosis.¹ The sedimentation rate is elevated in less than

25 per cent of patients and is more likely to be elevated in the bacteremic or the serologic type than in the localized type.

Histologic

In localized brucellosis, the finding of granulomas in infected tissue may be suggestive of the possibility of brucellosis—among other possibilities—but there are no histopathologic criteria by which brucellosis can be diagnosed with certainty. In cases of suspected brucellosis, tissue should be cultured because fluid—from a joint or purulent material from a draining sinus, for example—is sometimes negative for *Brucella* even though the organisms are present in the tissue.

Skin testing of individuals suspected of having brucellosis is not advised, because the correlation between the results of the test and the presence of the disease is low and because confusion may result from the ability of the test to induce antibrucellar agglutinins.

Roentgenographic Findings

In brucellar spondylitis, roentgenograms may reveal involvement of the intervertebral disks and contiguous vertebra, narrowing of the intervertebral space and eventual bony fusion of the adjacent vertebrae, narrowing with parrot-beak exostoses in the healing stage, or, rarely, paravertebral abscesses. In brucellar osteomyelitis the roentgenographic picture is that of medullary destruction, often with periosteal thickening. In brucellar bursitis and synovitis there is roentgenographic evidence of effusion and possible osteoporosis of adjoining bones.⁵ In brucellosis localized to the spleen, roentgenographic evidence of splenic calcification is almost the rule, and barium contrast studies⁶ may reveal the displacement of the gastrointestinal tract by the enlarged spleen. Brucellosis of the urinary tract may result in such urographic findings as calyceal destruction and pelvic dilatation, and areas of calcification may be discernible in the renal mass. As mentioned, pulmonary lesions may be detected on routine roentgenograms of the thorax, which on surgical extirpation and microbiologic study prove to be brucellar granulomas.

*See Test Your Word Score Page 1513.

Therapeutic Considerations

Antibacterial Drugs

Members of our group have continued to prefer use of a tetracycline in combination with administration of streptomycin in the management of most cases of brucellosis. With previous or current intolerance of streptomycin, less than normal renal function, or decreased auditory acuity, we give the tetracycline alone; but this has not been a common occurrence.

Up to the present, in the treatment of bacteremic and serologic brucellosis, we have used 500 mg. of a tetracycline given orally every six hours and 1 Gm. of streptomycin injected intramuscularly twice daily for two weeks. In chronic localized brucellosis, we have reduced the amount of streptomycin to 1 Gm. daily and have continued combined treatment for four weeks.

With the increasing number of potentially ototoxic drugs* and the possibility of auditory damage following their sequential use, we have considered the feasibility of reducing the amount of streptomycin employed in our antibrucellar regimens. In other words, a given patient may require administration of kanamycin for an infection of the urinary tract due to indole-positive *Proteus* organisms and also require vancomycin because of a serious infection due to *Staphylococcus aureus* (especially if he was allergic to the penicillins); then at a later date, he may have brucellar spondylitis. In such a patient there is some doubt whether the daily dose of 1 Gm. of streptomycin for four weeks should be administered. The converse is also applicable, where there is the need to prescribe kanamycin in a patient previously treated with full doses of streptomycin for such infections as brucellosis, tularemia, or enterococcal endocarditis. Consequently, we are considering reducing the daily dose of streptomycin to 1 Gm. in acute infection and to 0.5 Gm. in localized infection, and prolonging therapy an additional one or two weeks. The suggestion of Spink¹⁰ has considerable merit, wherein use of streptomycin should be discontinued after about 10 to 14 days, but therapy with the tetracycline alone should be continued for several weeks. The routine use of a tetracycline alone as an antibrucellar regimen is ob-

jected to because the duration of therapy must be prolonged considerably, the relapse rate in patients so managed may be significantly higher, and the fear that localized brucellosis at a later date may more likely occur in such patients. In patients receiving streptomycin, vestibular and auditory complications are best detected when audiometric and vestibular-turning tests are carried out before therapy, periodically during treatment, and again six months after treatment has been discontinued.

Surgical

The diagnosis of localized brucellosis most often depends on the procurement of material for culture, for example, from a site of osteomyelitis, from a removed spleen in which brucellar organisms have localized, or from an excised infected lymph node.

As a generalization, energetic surgical treatment for brucellosis of the skeletal system is required. An exception to this is brucellar spondylitis, in which the diagnosis almost always can be made by virtue of relatively high agglutination titers and in which the patient usually responds to rest, use of braces or casts, and antibiotic therapy. Of course, a coexisting paravertebral abscess would require surgical drainage. Infected joints and bursae respond well to excision of the synovial tissue and antibiotic therapy. Brucellar osteomyelitis is the hardest of all skeletal brucellar lesions to treat successfully and requires wide drainage and saucerization; unfortunately, secondary pyogenic infection often prolongs morbidity and makes management more difficult.⁵

Comment and Conclusions

Elimination of brucellosis in animals must precede ultimate eradication of the disease in man. Contact with infected animal tissues, ingestion of unpasteurized dairy products, and exposure to brucellar organisms in the laboratory have been the usual modes of human infection.

Contact with infected animals, and especially their products of conception, has been responsible for most human infections rather than ingestion of contaminated milk products. This accounts for the greater prevalence of the disease among such people as dairymen, meat-

packing employees, and veterinarians.

In the last few years, human brucellar infections have been found above the Arctic circle in Alaska.¹¹ Epidemiologic studies appear to indicate that the source of human infection is the caribou and the mode of infection may be ingestion of the infected animal's meat. In communities where caribou meat is consumed, five to 25 per cent of the residents have positive agglutination titers.

Since our initial encounter with the syndrome in 1956, members of our group have described 10 cases of localized brucellosis of the spleen.⁸ Our experiences to date indicate that the syndrome exists as a clinical entity apart from detectable brucellar involvement of other reticuloendothelial organs. This conclusion is based on the fact that the infection apparently has been restricted to the spleen in some cases and on the finding that antibiotic therapy may eradicate the infection in other reticuloendothelial organs but not in the spleen. That is to say, brucellar infection in such tissues as the liver and lymph nodes is eradicable in many cases by antibiotic therapy, but the infection may persist in the spleen despite such treatment and may be curable only by splenectomy. Also, splenectomy provides cultural proof of the suspected disease, removes any hypersplenic effect on the marrow, and allows detection of additional brucellar lesions (such as retroperitoneal abscess) that have occurred in such cases. In localized splenic brucellosis, cultural proof of the infection is especially desirable, since in half of our cases the *Brucella* agglutination titer has been negative or lower than that ordinarily considered as diagnostic.

In regard to patients suspected of having localized brucellosis, but in whom agglutination titers are not diagnostic, demonstration in their serums of blocking antibodies may be helpful.¹² Presence of such blocking antibodies corroborates suspicion of brucellar infection and may eliminate unnecessary operation in chronic infections without splenic involvement. Demonstration of increased amounts of the so-called antibodies in serum sedimenting as 7S globulins may be similarly corroborative of active brucellosis in such cases.¹³

In the rare individual who is unable to accept a tetracycline, one may consider use of drugs such as erythromycin, novobiocin, ampi-

cillin, and chloramphenicol. Erythromycin and novobiocin have given evidence of being efficacious.^{6,14} Chloramphenicol probably has an antibrucellar effect approaching that of the tetracyclines, but its routine use is not recommended because of possible hematotoxic effects. Use of ampicillin has not been sufficiently evaluated as yet.

In most patients with localized brucellar lesions, it is virtually impossible to precisely evaluate the results of antibiotic therapy be-

cause surgical procedures are carried out concurrently. A persistent question is whether antibiotic therapy should be given after surgical removal of what is apparently an isolated locus of brucellar infection. Although individualization of therapeutic effort is a function of the case at hand, we have often recommended antibiotic therapy in such instances. We have made such recommendations because we hoped to eradicate any residual infection in the locus and to subdue any other undetected, currently asymptomatic, area of brucellar residence.

References

1. Osmundson, P. J., Martin, W. J., Merritt, W. A., and Stroebel, C. F.: Brucellosis: Report of an Unusual Case. *Proc Staff Meet Mayo Clin* 32:58, 1957.
2. Martin, W. J., and Nichols, D. R.: "Chronic Brucellosis." In Wohl, M. G. *Long-Term Illness: Management of the Chronically Ill Patient*, Philadelphia, W. B. Saunders Company, pp. 513-517, 1959.
3. Schirger, A., Nichols, D. R., Martin, W. J., Wellman, W. E., and Weed, L. A.: Brucellosis: Experiences With 224 Patients. *Ann Intern Med* 52:827, 1960.
4. Martin, W. J.: Chronic Localized Brucellosis With Recurrent Constitutional Manifestations. (Editorial.) *Minnesota Med* 43:347, 1960.
5. Kelly, P. J., Martin, W. J., Schirger, A., and Weed, L. A.: Brucellosis of the Bones and Joints: Experience With Thirty-six Patients. *JAMA* 174:347, 1960.
6. Martin, W. J., Schirger, A., Kelly, P. J., and Beahrs, O. H.: Brucellosis. *Proc Staff Meet Mayo Clin* 35:717, 1960.
7. Martin, W. J., Nichols, D. R., and Beahrs, O. H.: Chronic Localized Brucellosis: With Recurrent Constitutional Manifestations. *Arch Intern Med (Chicago)* 107:75, 1961.
8. MacDonald, G. F., Martin, W. J., Wellman, W. E., and Weed, L. A.: Chronic Localized Brucellosis of the Spleen. *Postgrad Med* 40:703, 1966.
9. Weed, L. A.: Use of Selective Medium for Isolation of Brucella From Contaminated Surgical Specimens. *Amer J Clin Path* 27:482, 1957.
10. Spink, W. W.: *The Nature of Brucellosis*. Minneapolis, The University of Minnesota Press, 464 pp, 1956.
11. Brody, J. A., Huntley, B., Overfield, Theresa, M., and Maynard, J.: Human Studies of Brucellosis in Alaska. *J Infect Dis* 116:263, 1966.
12. Zinneman, H. H., Glenchur, H., and Hall, W. H.: The Nature of Blocking Antibodies in Human Brucellosis. *J Immun* 83:206, 1959.
13. Spink, W. W.: Host-Parasite Relationship in Human Brucellosis With Prolonged Illness Due to Suppuration of the Liver and Spleen. *Amer J Med Sci* 247:129, 1964.
14. Pfischner, W. C. E., Jr., Ishak, K. G., Neptune, E. M., Jr., Fox, S. M., Farid, Z., and Nor El Din, G.: Brucellosis in Egypt: A Review of Experience With 228 Patients. *Amer J Med* 22:915, 1957.

Life Span

People who wish they were as "strong as a horse" or as "contented as a cow" may be surprised to learn which mammal actually lives the longest. It is not the horse, not the cow, not the hippopotamus, not even the durable elephant. The longest-living mammal today is woman. The average girl can expect to live fully seventy-one years. The mighty elephant, once ranked as the longest-living mammal, now lags far behind with its sixty-year life span. The hippo has an expectancy of forty; the horse twenty to twenty-five; and the cow averages from nine to fifteen years. Even men live longer than elephants these days, an average of sixty-five years.

The turtle, which is not a mammal, lives at least a century longer than human beings. But the turtle can't brag about its advanced age and women probably won't, so we men are safe.

Cedric Adams, Minneapolis Tribune

Consciousness reigns but doesn't govern.—Valery

|| Varicose Veins

A
New
Surgical
Concept
in the
Treatment

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VARICOSE VEINS have been attributed to numerous causes. Many factors undoubtedly do play a role in their etiology. I feel, however, that one factor has been entirely overlooked, namely, a partial obstruction of the deep circulation in a relatively high percentage of cases. The obstruction occurs within the femoral sheath located just below the fossa ovale. In the light of these findings, I feel that varicose veins represent the development of collateral circulation as a bypass for the returning venous blood from the lower extremity to the external iliac veins.

About five years ago, several patients were observed with unilateral varicosities. In exploring the sapheno-femoral junction of these patients it was noted that the femoral lymph nodes were often enlarged. Where this was the case, the femoral sheath was found to be extremely tight, constricting the femoral artery and vein at or just below the level of the fossa ovale. It seemed only natural that one should open the femoral sheath and free up the femoral vein to facilitate the return of venous blood through the deep circulation. Following the incision of the sheath the internal and external saphenous veins were then stripped out. Much to my surprise, I found very little evidence of recurrent varicose veins postoperatively. In the past it was not uncommon to note the redevelopment of varicosities within a year or two following the stripping procedure. Since operating on more than one hundred cases in the past five years, I have been impressed with the lessened recurrence of varicosities where the fascia of the femoral sheath has been incised. A second constricting factor has been the presence of a small artery and vein running across the femoral fascia just below the edge of the fossa ovale. In a number of instances these vessels have been the chief constricting factor. In treating this problem we have cut and ligated the vessels in every instance and, in addition, have incised the fascia

longitudinally between the artery and vein. In doing so we have frequently noted that the femoral vein was constricted to about one third or even one fourth its normal caliber. Immediately after incising the fascia, the femoral vein has assumed its normal caliber. Recently venous pressure readings have been taken in the saphenous and femoral veins. The readings in the femoral vein have been taken below the sight of constriction and have revealed that the pressure within the vein is about 25 per cent higher than that in the saphenous vein.

History

From a historical standpoint the treatment of varicose veins has undergone an evolutionary process from simple ligation of the saphenous vein to extensive stripping and multiple ligations. In 1916 Homans first advocated sectioning of the saphenous vein. In 1927 Moschowitz suggested the combined ligation of the long saphenous vein with retrograde injections of the vein. Between 1927 and 1955 further progress in the combined surgical-medical treatment of veins was made. At the present time the accepted method is the stripping out of the entire internal and external saphenous system. In my hands the femoral fascia is also incised longitudinally to free up the deep circulation which has been found to be partially obstructed in about 40 per cent of our cases.

Surgical Technic

Skin Incision

A short incision is made in the upper thigh over the saphenous vein parallel to the groin and about two centimeters below the groin crease. All tributaries to the saphenous vein are first tied off and then the vein is cut distal to its insertion into the femoral vein. Next the femoral fascia is carefully inspected at the level of the fossa ovale. If a constricting blood vessel is present below the insertion of the saphenous vein into the femoral, this vessel is cut and tied.

Incision in Femoral Sheath

A vertical incision is made in the anterior femoral sheath between the femoral artery and vein for a distance of from two to four centi-

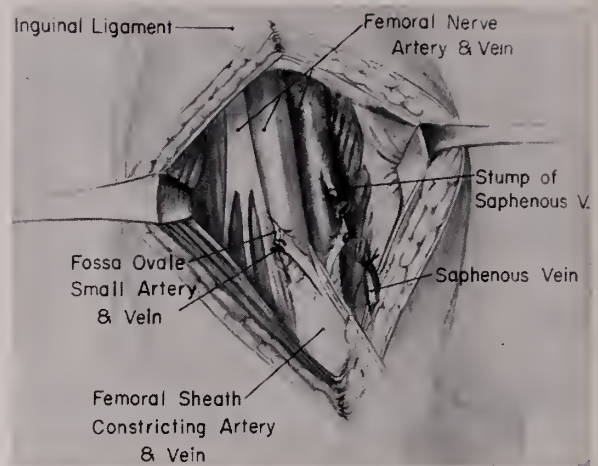


Fig. 1.—Technique of femoral fasciotomy in conjunction with internal saphenous vein stripping.

meters or until it fuses with the adventitia of the femoral artery and vein. See illustration. If one's finger can be passed easily beneath the femoral fascia at the fossa ovale no attempt is made to incise the femoral sheath. If this space will not admit the index finger, we have found that the femoral vein is definitely constricted.

Stripping the Vein

After completing the femoral fasciotomy a short incision is then made above the medial malleolus and an intraluminal flexible stripper is passed up through the entire length of the saphenous vein from the ankle to the groin. Then the vein is stripped out. Where perforations are encountered, additional incisions are made and the veins are tied off at the level of the fascia.

Conclusions

The femoral sheath is constricted in a relatively high percentage of patients having varicose veins. This constriction results in a partial obstruction of the venous return through the femoral vein. Incision of the femoral sheath from the fossa ovale down to its fusion with the adventitia of the femoral artery and vein is recommended. Where there are a small artery and vein crossing the fascia below the insertion of the vein, this vessel should also be incised and ligated. If this procedure is carried out in conjunction with a careful stripping out of the internal and external saphenous vein systems, very little recurrence of varicosities will be found during a five-year follow-up period.

References may be secured from the author or reprints.

Farm Accidents and Their Prevention

An Epidemiological Approach

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RECENTLY I WAS part of a team of physicians who treated a farmer from Nicollet County hospitalized because of a power take-off accident while harvesting soybeans. He had removed the safety shield from the power take-off shaft on his combine while repairing it and, while harvesting beans, had hurriedly jumped off his tractor and caught his heavy, loose clothing in the shaft. The result: multiple fractures of the left arm and amputation of portions of the left hand. He was unable to finish his harvesting, feed his cattle, or do his fall plowing. A man had to be hired to finish the harvesting, some of the cattle were sold at a loss, and this farmer's family suffered economic hardships, when at best, the economic situation of the family farm was tenuous. This story is repeated with variation time and time again throughout our state. This is a complex problem which has not only preventive medicine aspects, but complicated sociological implications as well. Modern agriculture presents unique problems to those engaged in medicine, especially preventive medicine. The farm population is diffuse. The home and the work place are the same. The work force is the whole family, male and female; the young son and the senior citizen. The activities are seasonal; the work techniques and jobs vary by individual; and the weather and climate play an important role. Because accidents are so common in the life of our rural patients and trauma results in a consumption of medical services, it behooves the physician, especially the rural family physician, to play a positive role in preventing these "preventable diseases."

Accidents play a leading role as the principal cause of death in all occupations. From ages one through 34, the leading cause of death is accidents. Agriculture is annually responsible for more occupational deaths than any other major industry in the United States. Three thousand lives were lost while men and women

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were working on farms in this country in 1965.¹ Fatal accidents comprise only a small proportion of the total accidents; for every death there are nearly one hundred serious, disabling, crippling injuries which require hospitalization.²

Although industrial death rates have declined significantly in the past several decades, agriculture, because of its individualistic nature, has not enjoyed such good fortune. The occupational death rate among farmers and farm workers has actually increased as noted below:

Accidental Deaths of Farm Residents by Year			
Year	Total	Farm Pop.	Death Rate
1950	15,500	25,058	61.9
1951	15,000	24,160	62.1
1952	14,500	24,283	59.7
1953	13,500	22,679	59.5
1954	12,500	22,099	56.6
1955	12,800	22,438	57.0
1956	12,800	22,362	57.2
1957	12,000	21,606	55.5
1958	11,600	21,388	54.2
1959	11,700	21,172	55.3
1960	11,300	20,541	55.0
1961	8,800	14,803	59.5
1962	8,800	14,313	61.4
1963	8,400	13,367	62.8
1964	8,300	12,954	64.1

Types of Accidents

Tractors

Machinery* is involved in two out of five deaths.⁷ It accounted for 51 per cent of the farm accidents in Minnesota in 1964.⁸ The tractor was involved in 90 per cent of the machinery accidents in Wisconsin in 1961.⁹ Tractor accidents claim the lives of an estimated 1,000 persons annually in the United States.¹⁰ Farmers drive tractors over rough ground at high speeds. Row crop tractors are driven over unsuitable terrain such as steep hillsides and loads are sometimes pulled from rear axle levels and above, thus predisposing to up-ending of the machine. *It is common practice to allow 10-year-old boys to drive tractors over highways and operate machinery with which they are not familiar. They often take their younger brothers and sisters for rides across fields and pastures and occasionally on the highways.* Farmers themselves may be

unaware of the potentially lethal nature of the tractor, and some are run over by their machines because of failing to disengage the engine before dismounting. Others are thrown from their machines while standing on the tractor. Tractors are operated upon the highways at night without proper lighting and reflectors. Below is noted the incidence of different types of tractor accidents in a National Safety Council study of 789 tractor fatalities.

Accident Type and Use of Tractor, 1964

Accident Type	%
Tractor upset	58
Fall from tractor	13
Crushed	9
Run over	8
Motor-vehicle collision	6
Power take-off	3
Other	3
Total	100

Use of tractor	%
Tillage, planting, harvesting	29
Tractor enroute to site	15
Material handling	15
Towing vehicle or implement	11
Passenger transportation	6
Clearing land	4
Stationary power source	4
Other	16
Total	100

Harvesters

Harvesting machinery accounts for most of the farm accidents involving machinery other than tractors. Every fall farmers fall prey to the snapping rolls of the cornpicker. The pickups of combines and haybalers also manage to maim the extremities of countless other farm workers. *Most of these injuries are due to leaving the machinery running while cleaning and servicing.* Often safety shields over drive belts, power shafts, and chains are missing because repairs have been made haphazardly during the periods of peak machine use. Both the age of the machine and the familiarity with its operation are important. In the Dane County study in Wisconsin in 1958, it was found that nearly one fourth of the accidents involving machinery could have been avoided by replacement of worn, loose equipment and the proper use of the machinery.¹²

*Tractor, mower, haybaler, cornpicker, combine, power saw, ensilage cutter, and manure spreader.

Falls

According to most sources falls appear to be the second largest cause of farm accidents and accounted for one fifth of the farm accident fatalities in Minnesota in 1964¹³ and for 27% of the non-fatal injuries in the Dane County study in Wisconsin.¹⁴ Nearly one half of these falls occurred from hay wagons and tractors. Falls from trees, ladders, machinery, and on slippery terrain also account for a large number of accidents. As can be expected, many of these falls occur in and around the home, barnyard, and service buildings. *Unstable, old, wornout ladders, weak hay wagon floors, lack of handholds on machinery, and wet floors greatly increase the chance for a disabling fall.*

Burns

Burns from fire and explosion of combustible material are the third leading cause of farm fatalities due to accidents according to the United States Public Health Service.¹⁵ This has also been true in Minnesota over the last decade.^{16,17} Most of the burns are due to fires and explosions caused by defective or misused electrical equipment, defective heating units, sparks from tractors and rubbish on manifolds, and careless handling of greases and petroleum fuel. *Common offenses include: tractors refueled without shutting off the engine, trash and rubbish accumulating around the farm shop, granary, or barn; and inadequate or defective lighting used around service buildings.*

Animals

Another common accident agent is the farm animal,^{18,19,20,21} involved in an average of 15 per cent of all farm accidents. These accidents frequently involve handling bulls, saddle horses, loose cattle, and small children in animal enclosures such as hog pens.

Tools

Other agents less commonly associated with farm accidents include blows from falling objects, hand tools, poisoning with farm chemicals, and ingestion or inhalation of food or other objects causing obstruction or suffocation. The scope of agents directly related to

the home, drownings, or the family automobile is too wide for this presentation.

Environment

Seasonal

As in any epidemiological study, the environment is an important factor. Environmental factors important in the genesis of farm accidents include: weather, climate, season, temperature, terrain, time of day, length of working hours, lighting, and work area. The incidence of all rural accidents rises rapidly during the summer months and then falls abruptly with the completion of harvest. July and August annually show the greatest percentage of farm accidents.²² This is corroborated by studies done in Minnesota. Thompson noted that rural accidents reached a spring peak in May and a top peak in July, declined in mid-summer, and reached a third peak in October. These peaks seem to correspond to the three common periods of farm work: spring fieldwork, haying and harvesting, and corn picking.²³ Weather appears to have little effect on the rate of accidents; however, one would certainly expect an increase during periods of fog, impending storms, and extreme heat.

Farm Yard

According to the Dane County study done in 1960, nearly 55% of all reported accidents occurred in the barn or around the farmyard²⁴ involving animals, fires and explosions, falls, and blows by falling objects. Poor lighting, dilapidated buildings, slippery footing, and inadequate electrical wiring play a role in these areas. Rough and steep terrain play a part in tractor accidents in fields and pastures. The Dane County study also reports that time of day would also seem to show a relationship to the incidence of farm accidents. There is a definite mid-to-late morning and mid-to-late afternoon increase of accidents with peak hours of 11 a.m. and 5 p.m. Longer working hours during the peak harvest seasons predispose to fatigue, as do lack of rest periods during the day. The individual farmer, who is his own manager and owner, is all too prone to push his work force, namely himself and his family, beyond normal limits.

The Farmer Himself

Perhaps the most important aspect of the epidemiological study involves the host, namely the farmer, his hired help, and his family. Important factors include age, sex, experience, safety education, physical status, fatigue, drugs and medications, accident proneness, and that difficult to evaluate factor, carelessness.

His Children

Thirty to 40 per cent of all farm accidents occur to children and teenagers. According to the National Safety Council one fourth of all tractor victims are under 20 years of age.²⁵ Children are also involved in a major portion of death by drowning and firearms, and in accidents with farm animals. Accidents involving farm machinery are perhaps even more tragic when they involve the life or extremity of a child. It would seem that natural curiosity and lack of respect for dangerous machinery coupled with parental irresponsibility and poor judgement are responsible for these accidents. A child has no reason to be around an operating piece of farm equipment or large farm animals. The best control of this problem, according to Lucas and Wirka at Wisconsin, would be for the farmer to divorce his children from his work around machines as the factory worker does.²⁶ In studies done in Minnesota, the bulk of accidents occurred to persons between 15 and 30 years of age; and the male members of the family stood the greater chance of becoming injured, especially the husband and the son.²⁷

The Hired Help

This lack of trained, experienced labor increases dangers in operating machinery alone and caring for unruly animals. It also means that unskilled, inexperienced members of the farm family are needed to operate machinery and perform dangerous tasks during peak work periods. Often there is a lack of supervision for this unskilled labor, and there is no one to supervise safety practices with even the experienced farm worker.

Fatigue

Fatigue is a major factor in farm accidents.

The farm worker works on his own time and often without interruption. The physical status of many farm workers is unknown. There may be problems involving sight, hearing loss, disabilities, or systemic disease which may enhance the fatigue factor. At times the farmer is unaware of the effects of medications he may be taking which can cause drowsiness, incoordination, and slowed reaction time. Accident proneness, a relatively new concept in the field of accident prevention, plays an indeterminate role in the genesis of agricultural accidents. Industrial studies show that the chronically depressed, neurasthenic, and low-normal intelligence groups have increased numbers of accidents. This probably can be applied accurately to agriculture.

Carelessness

Intimately involved with fatigue and accident proneness is the factor of carelessness and haste. Forty-five per cent of those interviewed in the Dane County study were in a hurry at the time of the accident.²⁸ *Carelessness is probably the largest and most significant factor underlying farm accidents.* Careless repair, simple neglect of equipment, poor judgement in its use, high speeds, and lack of preparation for emergencies all predispose to major proportion of our accidents.

Prevention

Education

The first definite programs of farm safety education were instituted in Minnesota in the early 1930s through the Agricultural Extension Service and the 4-H Clubs. Many rural organizations such as the Farm Bureau and Farmer's Union carry on safety campaigns with educational speeches, demonstrations, and spot announcements in the mass media. Local county extension services and rural Parent-Teacher Associations feature "Farm Safety Night." This year the National Safety Council and U. S. Department of Agriculture sponsored the twenty-third "National Farm Safety Week" focussing national attention on agricultural safety. This "Farm Safety Week" is also complemented by state "Farm Safety Weeks." Perhaps the most effective programs of farm

safety occur in the farm safety projects of 4-H Clubs, high school vocational agriculture classes in farm safety, and adult vocational agricultural classes. These farm safety projects provide extremely worthwhile practice and make participants aware of the many ramifications of accident prevention.

Engineering

In the area of machinery design, it must be conceded that manufacturers build machinery that the farmer will buy on the basis of performance and cost. In recent years more time has been spent by manufacturers in educating the farmer to use his equipment safely by demonstration and increased information in the operator's manual. State agricultural extension services have also made great efforts in promoting design of safer machinery and farm buildings.

Enforcement

Enforcement, which has given great rewards in industrial safety programs, breaks down in agriculture because usually the activities are carried out by the owner-operator on his own premises. Scattered attempts have been made at routine inspection of farm premises by Future Farmer groups and 4-H clubs to detect potential hazards; but in general, these methods of health promotion leave much to be desired. Farm leaders, however, continue to stress education as the most important line of attack.

What more is to be done? A beginning has been made. The first institute of agricultural medicine was established in Poland 15 years ago. The Institute of Agricultural Medicine at the State University of Iowa College of Medicine was established in 1955 to examine the problems of agricultural health, among them farm accidents. Since then, this Institute has made meaningful studies of rural health problems, invented countless safety devices, and most of all, evolved a multidisciplinary approach to agricultural preventive medicine. They have brought together under one aegis physicians, veterinarians, toxicologists, safety engineers, sanitary engineers, and people skilled in anthropology-sociology to study all the elements involved in the detection, evaluation, and control of agricultural health and safety prob-

lems. This "intramural" group is then supported by the community professional group, the "extramural" group, who can actually apply preventive measures.³⁰

Teaching in Schools

Coupled with research and study, there must be an increase in long-range safety and health education to create health and safety consciousness in individuals during a period in their lives when these habits can most readily be taught and accepted—in childhood. Health and safety education must be interwoven into every aspect of the school curriculum. More efforts should be made by manufacturers to protect the farmer in spite of himself. It is important that the operation and maintenance aspects have the highest design priority; i.e., the machine should be built around the man instead of the man around the machine. In addition to increased safety design, the farm worker must be "re-designed." More attention needs to be paid to workman's compensation laws, pre-employment physical examinations, safety training, and fitting the job to the individual. Ideally, changes in working hours, rest periods, and environmental hazards such as dust and noise could be made.³¹

Physician

The rural physician who treats farm accident victims and who renders medical care to their families is in a key position to help reduce their accidents. Printed literature can be available in the waiting rooms, and the physician should never pass up opportunities to advise and instruct safe practices.³² The rural physician must have an awareness of potential accident situations and a community interest in preventing "dis-ease." The need to protect children should be discussed with the farmer and his family. Specific measures for prevention include regular searches for physical defects, correction of those defects, and recommendations for limitations of activities beyond capabilities, especially for the senior citizen. The physician must also support his regional Agricultural Health Institute with information and help disseminate safety information as part of his local professional society. The rural physician should also be ready to minimize the conse-

quences of farm accidents, should they occur. Emphasis can be placed on pre-payment health and accident protection, welfare services, and community rehabilitation services.

Conclusions

It is a known fact that farm accidents can be decreased by an epidemiological approach. Indeed, the potential for reducing the mortality and morbidity is greater here than in cardiovascular, renal, or malignant disease. Presentation of known factors involving the agent, the host, and the environment along with proposals

for increased health promotion and specific protection provides a simple, logical way for the rural physician to approach this complex problem at the local level.

Agriculture is responsible for more occupational deaths than any other major industry in the United States. Farm machinery, falls, burns and explosions, and farm animals are common agents. Environmental factors include weather, climate, and work areas, and time of day. Accident prevention is based on the traditional "E's" of safety: education, engineering, and enforcement.

References

1. United States Department of Agriculture. Farm Resident Accidents, 1965. Farm Safety Review. 24:9, 1966.
2. Ibid.
3. Ibid.
4. Ibid.
5. Ibid.
6. Walsh, L. G., Chalkley, I. H. F. and Evans, A. S.: Nonfatal Farm Accidents. Wisconsin Med J 57:118, 1958.
7. National Vital Statistics Division. Accidental Farm Deaths by Source and Age, 1963. Farm Safety Review. 23:10, 1965.
8. Minnesota Department of Health. Farm Accident Fatalities Occurring in Minnesota by Type, 1964.
9. Lucas, G. L., and Wirka, H. W.: Farm Accidents Occurring in Children. Wisconsin Med J 62:405, 1963.
10. National Safety Council. Tractor Fatalities. Farm Safety Review. 24:10, 1966.

11-32 May be secured from the author or the reprints.

"I Wish My Hands Were as Skillful as That"

A boy in short trousers at the turn of the century, enthralled with the romance of the woods, hills and marshes, decided he was going to be a field naturalist. At sixteen he had become quite adept with scalpel and museum techniques, thanks to an older brother of his best friend across the road, who collected everything from snakes to skunks and had a museum of his own. Stammering kept the boy out of school for two years and he lived all the more in this naturalist's world, hunting alone afield and at home learning to organize, label and classify. On a fishing trip at seventeen he met a celebrated surgeon, who, leaning over and watching the boy skin a short-tailed shrew, remarked: "I wish my hands were as skillful as that." The boy's determination to be an explorer and a naturalist wavered under this compliment. The thought of being a surgeon took root. Next year at college he took biological and premedical courses, and practically committed himself to a medical future, but his parents were skeptical because of the stammering. Efforts at trying to cure the stammer developed an interest in "nerves" and psychology, which was stimulated by his professors—Parker, Munsterburg and Holt. By senior year the decision was formed to go to medical school and study neurology and psychiatry.*

*Stanley Cobb (1887-) in WHY WE BECAME DOCTORS, edited by Noah Fabricant, M.D., 1954.

Gout

Gout is the distemper of a gentleman; whereas the rheumatism is the distemper of a hackney-coachman, who is obliged to be out in all weathers and at all hours.—Lord Chesterfield

Polymyalgia Rheumatica

Report of Seven Cases

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POLYMYALGIA RHEUMATICA is a clinical syndrome characterized by muscular pains in the girdle area and an elevated sedimentation rate, and is a frequent prodromal or concomitant feature of giant cell arteritis. Polymyalgia rheumatica is diagnosed by the clinician, often by exclusion. Giant cell arteritis is a pathological diagnosis.

Polymyalgia rheumatica and giant cell arteritis have numerous similarities. In each, the duration of the disease is usually two to four years. Clinical manifestations are comparable. Both diseases have a high sedimentation rate with few other significant laboratory findings. Either can have ocular complications including blindness. Each responds to corticosteroids. Although some believe the diseases are not related¹⁻³, there is increasing evidence, especially through temporal artery biopsy, that polymyalgia rheumatica is associated with giant cell arteritis⁴⁻⁹.

Polymyalgia rheumatica has been described frequently in European literature^{1-7,10-13} but only rarely in American.^{8,9,14,15} Although other terminology has been suggested in the past, Barber first suggested the term "polymyalgia rheumatica" in 1957¹⁰. The disease incidence has been considered⁵ commensurate with gout⁷ in the older age groups, and is felt to be a collagen disease¹.

It is characterized by rather acute muscular aching of the neck, shoulders, back, and thighs^{1,6,8-12}. There may also be headache, malaise, lethargy, fever, sweating, and anorexia. The sedimentation rate is usually elevated over 100 mm. per hour.^{5,6} There may also be slight anemia, leukocytosis, decrease in albumin and increase in alpha globulin^{1,5,6,11}. Other collagen disease and carcinomatosis may have to be excluded, although some feel that examinations for malignancy are unnecessary after becoming familiar with the disease⁵. Pathological studies of a few autopsied cases have shown little^{3,16}. Deltoid muscle biopsy has been negative^{1,11} and shoulder joint biopsy has shown only chronic inflammation².

Complications are related to ischemic effects

of associated arteritis and include brachial artery occlusion^{6,13}, Takayasu's disease (axillary artery occlusion)⁵, retinal artery occlusion producing blindness⁸ and third or sixth cranial nerve involvement producing ophthalmoplegia⁴. Symptomatic treatment includes bed rest, salicylates and phenylbutazone^{10,11,12}. Distinct subjective improvement occurs with corticosteroids and is felt to decrease vascular complications including ischemic changes of the eye and brain⁵. Polymyalgia rheumatica is usually self-limiting with a two to four-year duration^{6,10,11}, though the course may be protracted^{6,9}.

In the past few years we have had a chance to observe seven cases of polymyalgia rheumatica in our practice.

Case Report

Case 1

The first case has been previously reported.⁸ This 75-year-old woman, seen in January, 1964, had excruciating soreness of the muscles of her neck, shoulders, back, and thighs. Sedimentation rate was 110 mm. Diagnosis was uncertain and hospitalization was considered. The patient suggested the diagnosis, polymyalgia rheumatica, after studying the disease in her nephew's medical library. In July, 1964, she suddenly lost the sight of her left eye from apparent cilioretinal artery occlusion. Biopsy of a firm but non-tender temporal artery showed giant cell arteritis. Forty to five mg. of prednisone daily controlled the myalgia and sedimentation rate which fell from 70 to 30 mm. in two weeks. Although left blindness remains, she has otherwise done well. She has had three episodes of erythematous swelling of the ears relieved by tetracycline.

Comment

Polymyalgia rheumatica was diagnosed three months after the onset of myalgia. Four months later left blindness occurred from retinal artery occlusion. Asymptomatic (temporal) giant cell arteritis was then

proved on biopsy.

Case 2

Another case of polymyalgia rheumatica was diagnosed retrospectively. This 72-year-old widow was seen in 1960 with a three-month history of severe pains in the lumbar region, hips, thighs, and neck. Pain was so bad in the morning that she had to ease her way out of bed. She had a past history of unoperated cholelithiasis. Physical examination was non-contributory. Hemoglobin was 10.3 grams, sedimentation rate 108 mm. (Westergren) and white blood count 14,650 with 57% neutrophils. Serum proteins showed 1.9 grams albumin and 4.7 grams globulin. Bence Jones protein and bone marrow examinations were negative.

It was felt that the patient had an unusual collagen disease. She was treated with vitamins, hematinics, and analgesics. Although lost to follow-up, it is known that she made a slow recovery in the following years.

Comment

After other diseases were excluded, retrospective study of this patient suggests polymyalgia rheumatica.

Case 3

This 75-year-old woman was seen in July, 1965, with the abrupt onset of aching of the right shoulder, right arm, and thighs. Physical examination was negative. Hemoglobin was 12.7 grams, sedimentation rate 88 mm. and fluorescent anti-nuclear antibody positive 1:10 (not definitely significant). Temporal artery biopsy was negative. It was felt she had polymyalgia rheumatica. The patient's aching disappeared with prednisone which was continued in doses of 5-20 mg. daily. Sedimentation rate dropped to 24 mm. in three weeks. She developed a persistent blurring of her left eye. Ocular examinations showed only minimal cataracts and arteriosclerosis. Although ample doses of prednisone kept her essentially symptom-free and kept the sedimentation rate down, her course was interrupted by falls producing a fractured hip in September, 1965, and fractured arm in March, 1967.

Comment

The patient had typical polymyalgia rheumatica including myalgic and sedimentation rate response to corticosteroids. Temporal artery biopsy was negative.

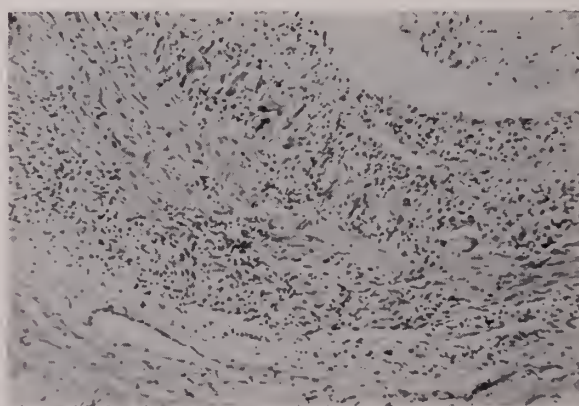
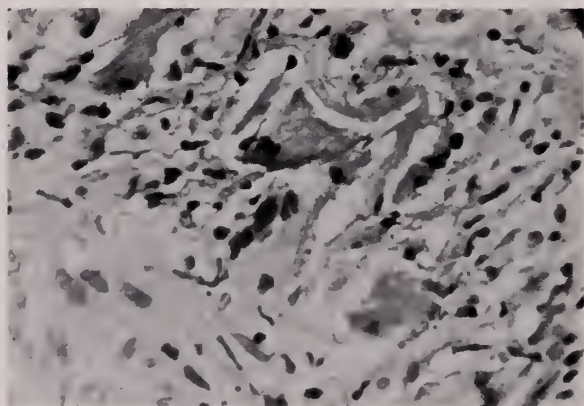


Fig. 1 — Sections of temporal artery showing mononuclear infiltration and multinucleated giant cell.

Case 4

In August, 1965, this 74-year-old woman developed back and hip pain so that she had difficulty getting in and out of bed. In November she noted blurred vision, episodic vertical diplopia and mandibular pain. Physical findings were negative, except for a constricted left field of vision. The left fundus showed a few flame-shaped hemorrhages and elevation of the disc, consistent with optic neuritis. Hemoglobin was 12.0 grams and sedimentation rate 78 mm. Electroencephalogram showed mild diffuse abnormality. Cerebrospinal fluid, skull x-rays, and carotid angiography were negative. Fluorescent anti-nuclear antibody was positive 1:320. Temporal artery biopsy was negative. Impression was optic neuritis associated with arteritis. She was treated with corticosteroids.

The patient was examined at the Mayo Clinic in January, 1966. The left field of vision remained constricted and the nerve head was pale with surrounding glial tissue and pigment disturbance. They agreed with the diagnosis of temporal arteritis. Prednisone was continued. In March, 1966, the sedimentation rate was 6. After discontinuing prednisone in July, 1966, the patient had more pain in the hips and thighs. In March, 1967, hemoglobin was 12.6 grams and sedimentation rate 38 mm. No medication was used.

Comment

Although myalgia of the back and thighs preceded by two months the dominant ocular features of her disease, they were an important symptom and were relieved with corticosteroids.

*Dr. Frederick H. Lott, Pathologist.

**Attending physician, T. J. Catlin.

Case 5

In June, 1966, this 82-year-old woman began having arthralgia of the neck, back, and thighs. Indocin and butazolidin were not effective, though aspirin gave some relief. In September, 1966, she had a loss of vision in the left eye which was felt by an oculist to be vascular in origin. Medical evaluation showed diminished right and non-pulsating left temporal arteries. Sedimentation rate was 80 mm. Left temporal artery biopsy revealed giant cell arteritis (Figure 1).^{*} The patient was treated with 20 mg. prednisone daily. When seen in three weeks she had lost all her stiffness and felt much better. Her vision, however, did not improve. She could make out the figure of a picture with her left eye only. Sedimentation rate was 19 mm. The prednisone was cut to 15 and later 10 mg. daily. Myalgia was readily controlled. Her convalescence was complicated by a fall in a bus in which she suffered a fracture of her pelvis and later intervertebral disc symptoms.

Comment

Girdle arthralgia preceded unilateral blindness and biopsy-proven giant cell temporal arteritis.

Case 6**

This 74-year-old woman became ill in July, 1966, with frontal headache and stiffness and pain in the posterior neck and shoulders. She noted pain and pressure of the left temporomandibular joint; aggravated by chewing. She developed low-grade fever and left pleural effusion. Sedimentation rate was 109 mm., hemoglobin 12.9 grams, and white blood count 24,950 with 78% neutrophils. Twenty mg. of prednisone was given daily. The myalgia improved.

TABLE I
CLINICAL FEATURES IN SEVEN WOMEN WITH POLYMYALGIA RHEUMATICA

CASE	I	II	III	IV	V	VI	VII
AGE	75	72	75	74	82	74	54
MYALGIA	Neck, shoulders, back, and thighs	Neck, back and thighs	Shoulder, arm and thighs	Back, thighs, and jaw	Neck, back and thighs	Neck, shoulder and jaw	Back, & chest
FEVER °F.	99	100	99.2	100.2	98	100	100.6
Gm. Hemoglobin	12.3	10.3	12.7	12.0	11.5	12.9	11.9
F.A.N.A.	—	—	1:10	1:320	—	—	Negative
SED RATE CHANGE WITH PREDNISONE	110 to 30	108 (not treated)	88 to 24	78 to 16	80 to 19	109 to 55 and 9	108 to 38
TEMPORAL ARTERY PULSATION	Decreased	Normal	Normal	Normal	Decreased	Normal	Normal
TEMPORAL ARTERY BIOPSY	Positive	None	Negative	Negative	Positive	None	Negative
VISUAL COMPLICATIONS	Left blindness	None	Blurred vision cause unknown	Optic neuritis; constricted left field	Left blindness	None	None

When hemorrhage occurred from acute gastritis, corticosteroids were stopped. Soon there was increased myalgia, temporal pain and right hemiparesis lasting 24 hours. With resumption of prednisone she felt much better. Leukocyte count remained elevated with values from 14,600 to 23,200. Successive sedimentation rates were 55, 45, 31, and 9 mm. The patient remains asymptomatic on 10 mg. of prednisone daily.

Comment

This patient had apparent polymyalgia rheumatica with symptomatic temporal arteritis complicated by probable cerebrovascular insufficiency producing transient hemiparesis.

Case 7*

This 54-year-old woman was seen first in 1965 with exhaustion, chills, fever, abdominal pain, and weight loss. Events in her past health included tonsillectomy, appendectomy, hysterectomy, cholecystectomy, thyroidectomy for hyperthyroidism and subsequent hypothyroidism. Physical examination showed no abnormalities. During hospitalization her temperature was 99.6 to 100.6 F. X-ray survey was negative. Hemoglobin was 11.9 Gm., sedimentation rate 108 mm., serum proteins normal except for a slight increase in alpha globulins, and T-3 9.6% (normal range 10.3 to 14.3%). LE prep, bone marrow, and fluorescent anti-nuclear antibody tests were negative. Retroperitoneal sarcoma was considered but abdominal exploration was negative. Peritoneal biopsy showed chronic inflammation and fibrosis. The patient was maintained on supplemental thyroid.

She continued to have low-grade fever and began having headaches, back pain, and chest pain. Sedi-

mentation rates varied from 40 to 80 mm. In November, 1966, a daily dose of 20 mg. of prednisone was started. She felt better and the sedimentation rate dropped to 10 mm. She discontinued prednisone and her aching returned in the head, neck, arms, and legs. Sedimentation rate was 37 mm. At this time biopsy of a normally pulsating temporal artery was negative. Prednisone was resumed and she has remained symptom-free.

Comment

Abdominal symptoms initially dominated her disease. Myalgia consistent with polymyalgia rheumatica occurred later. There was favorable response of myalgia and sedimentation rate to prednisone.

Discussion

Seven cases of polymyalgia rheumatica are reported. All were women, ranging in ages from 54 to 82 years. Sedimentation rates varied from 78 to 110 mm. When followed, sedimentation rates decreased markedly on prednisone. Three had definite visual complications. Two of five with temporal artery biopsy showed giant cell arteritis. Temporal arteritis is known to be patchy in "skip" areas so that a negative biopsy does not exclude the disease⁹. Two patients had falls producing serious fractures. Table 1 reviews the clinical features. The features in reported polymyalgia rheumatica are summarized in Table 2. These

TABLE 2
CLINICAL FEATURES IN REPORTED SERIES OF POLYMYALGIA RHEUMATICA

AUTHOR	YEAR	FEMALE	MALE	TOTAL	AGE	SED. RATE (WESTERGREN)	EYE COM- PLICATIONS	POSITIVE ARTERY BIOPSY TEMPORAL
BARBER ¹⁰	1957	10	2	12	46-68	45-110	None	—
GORDON ¹¹	1960	11	10	21	49-82	42-122	None	—
BOYLE & BEATTY ¹	1961	13	8	21	46-76	17-71 (Wintrobe)	None	—
TODD ¹²	1961	16	4	20	61-78	75-138	None	—
ALESTIG & BARR ⁵	1963	5	5	10	55-88	24-147	None	7 of 10
GORDON et al. ²	1964	1	5	6	54-82	49-92	None	—
HAMRIN et al. ^{6,13}	1965	29	23	52	52-85	64-155	None	21 of 48
DAVISON et al. ³	1966	11	3	14	55-78	60-123	None	—
DIXON et al. ⁷	1966	26	5	31	50's-90's	Most over 80	9	13 of 31
WILSKE & HEALEY ⁹	1967	17	1	18	52-75	73-132	1	3 of 12
CURRENT SERIES	1967	7	0	7	54-82	78-110	3	2 of 5
TOTAL		146	66	212	46-90	24-147	13 or more	46 of 106

*Attending physician, Dr. Olin M. Odland.

include the predominance of women, older age, high sedimentation rate, eye complications, and numbers showing giant cell arteritis on temporal artery biopsy.

Summary

The clinical syndrome of polymyalgia rheu-

matica is reviewed and seven cases reported. It would appear that polymyalgia rheumatica is a frequent concomitant feature of giant cell arteritis in a systemic collagen disease. Both diseases should be treated with corticosteroids to decrease ischemic complications including blindness.

References

1. Boyle, A. C., and Beatty, D. C.: Polymyalgia Rheumatica. *Proc Royal Soc Med* 54:681, 1961.
2. Gordon, I., Rennie, A. M., and Branwood, A. W.: Polymyalgia Rheumatica. *Ann Rheum Dis* 23:447, 1964.
3. Davison, S., Spiera, H., and Plotz, C. M.: Polymyalgia Rheumatica. *Arthritis Rheum* 9:18, 1966.
4. Paulley, J. W., and Hughes, J. P.: Giant-cell Arteritis, or Arteritis of the Aged. *Brit Med J* 2:1562, 1960.
5. Alestig, K., and Barr, J.: Giant-cell Arteritis. A Biopsy Study of Polymyalgia Rheumatica, Including One Case of Takayasu's Disease. *Lancet* 1:1228, 1963.
6. Hamrin, B., Jonsson, N., and Landberg, T.: Arteritis in Polymyalgia Rheumatica. *Lancet* 1:397, 1964.
7. Dixon, A. S., Beardwell, C., Kay, A., Wanka, J., and Wong, Y. T.: Polymyalgia Rheumatica and Temporal Arteritis. *Ann Rheum Dis* 25:203, 1965.
8. Nuessle, W. F., Miller, H. E., and Norman, F. C.: Polymyalgia Rheumatica, Giant-cell Arteritis and Blindness: A Review and Case Report. *J Amer Geriatr Soc* 14:566, 1966.
9. Wilske, K. R., and Healey, L. A.: Polymyalgia Rheumatica. A Manifestation of Systemic Giant-cell Arteritis. *Ann Intern Med* 66:77, 1967.
10. Barber, H. S.: Myalgic Syndrome With Constitutional Effects. Polymyalgia Rheumatica. *Ann Rheum Dis* 16:230, 1957.
11. Gordon, I.: Polymyalgia Rheumatica. A Clinical Study of 21 Cases. *Quart J Med* 29:473, 1960.
12. Todd, J. W.: Polymyalgia Rheumatica. *Lancet* 2:1111, 1961.
13. Hamrin, B., Jonsson, N., and Landberg, T.: Involvement of Large Vessels in Polymyalgia Rheumatica. *Lancet* 1:1193, 1965.
14. Levey, G. S., Carey, J. P., and Calabro, J. J.: Polymyalgia Rheumatica: A Separate Rheumatic Entity? *Arthritis Rheum* 6:75, 1963.
15. Polasky, N., Polasky, S. H., Magenheimer, H., and Abrams, N. R.: Giant-cell Arteritis. Review and Report of Case. *JAMA* 191:341, 1965.
16. Bagratuni, L.: Prognosis in the Anarthritic Rheumatoid Syndrome. *Brit Med J* 1:513, 1963.

Medical Men on Postage Stamps

Leon Calmette (1863-1933) was a French bacteriologist and co-developer with *Camille Guérin* (1872-1961) of the tuberculosis vaccine BCG (*Bacillus-Calmette-Guérin*). Calmette also introduced a serum for snake bite and described the ophthalmic tuberculin reaction. Among several countries issuing postage stamps in commemoration of Calmette's and Guérin's joint achievement were France in 1948, Belgium in 1953, and St. Pierre Miquelon in 1963.

Nicolas Gutierrez (1800-1890) was a Cuban anatomist, surgeon and medical writer, who started Cuba's first medical organ, *El Repertorio Medico Habanero*. Recognition was awarded his pioneer work in medical journalism by the issuance of a Cuban postage stamp in 1940.

Remedies for Broken Bones

For broken bones, a sovereign remedy is the ashes of the jaw-bone of a wild boar or swine: boiled bacon, too, tied round the broken bone, unites it with marvellous rapidity. For fractures of the ribs, goats' dung, applied in old wine, is extolled as the grand remedy, being possessed in a high degree of aperient, extractive, and healing properties.

Thinking is more interesting than knowing, but less interesting than looking.—Goethe

How Long Can One Live*

One side of the longevity problem is determined by social factors. But there is another side to it, which is based on biological laws.

A great many men live to be ninety, a hundred, and even more. The greatest number of people over a hundred live in the Soviet Union. The 1926 census placed them at about 7,000. Fifty-five of them lived in Moscow. Bulgaria was second with 158. There were 86 in Germany, 58 in Sweden, and 51 in Italy. In Norway, which is to all appearances a country of strong men and women, there were only 35 people of a hundred and over.

In 1937 the Ukrainian Institute of Clinical Physiology found several old men aged 130, 135, and 142 in Abkhasia. In 1936 mountaineer Khapara Knut died in Abkhasia's Ochemchiry District at 155. He had been the oldest man in the world. In August 1949 Vasily Tishkin, a Stavropol collective farmer aged 144, took a holiday at the Central Trade Union Council's Sanatorium No. 22.

Hundred-and-forty-eight-year-old Mahmud Bagir ogly Eivazov works at the Komsomol Collective Farm in Azerbaijan. In March 1956, when he celebrated his 148th birthday, he was awarded the Order of the Red Banner of Labor for his meritorious work in collective farming.

But many people live no longer than 80-85 years. Many more live only 60-70 years. And quite a few die at 45 and 50.

It is natural to ask how long a man could really live. . . . Buffon, who lived in the 18th century, proposed an original method of calculating the answer. He determined how long domestic animals grow by watching the growth of their bones. That was easy. An organism is full-grown when its bones stop increasing in length. A dog, Buffon established, grows two years, a cat—18 months, a cow—four years, a horse—five, and a camel—eight, etc. He then divided the life span of each animal species by its period of growth. This yielded a mean figure of six, leading him to the conclusion that the life span of any higher mammal, including man, is five-six times longer than its period of growth. According to him, therefore, man's normal physiological life span is 150 years, or six times his period of growth, which lasts about twenty-five years.

*L. Fridland, M.D.: *The Achievement of Soviet Medicine*, 1961, edited and translated from the Russian by W. Horsley Gantt, M.D.

Pioneer Anesthesia with Cold

Hippocrates of Cos, the great physician who was born about 459 B.C., used his considerable powers to find effective ways of easing pain. He is said to have used *cold* as a means of producing insensitivity. He would numb a limb by packing it in ice or snow before performing the operation.

Pain relief by chilling was reintroduced in 1646 by the Neapolitan physician and anatomist, Marco Aurelio Severino. The technique used was described by Thomas Bartholin of Denmark in his book, *The Medical Use of Snow*.

"Before employing cautery on wounds in various parts of the body, apply snow to dull the sensation. Severino had to apply the medication in narrow parallel lines; after a quarter of an hour the feeling would be deadened and the part could be cut out without pain."*

*Bernard Seeman: *Man Against Pain*.

Bacteremia and Candida Septicemia

Review
of
185 Cases
During
A
Four-Year
Period

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SINCE THE INTRODUCTION of antibiotics the number of serious staphylococcal infections, particularly those occurring within hospitals, has greatly increased.¹⁻³ More recent attention has been drawn to the increase in gram-negative bacterial infections and to systemic mycoses.^{1,3-6} It seemed worthwhile to review the cases of bacteremia and fungemia seen at Minneapolis Veterans Hospital during a four-year period with regard to underlying host factors, source of infection, etiologic agent and the role of antibiotics and other chemotherapeutic agents in the occurrence and course of these infections.

Materials and Methods

This retrospective study encompasses 185 patients with proven bacteremia or fungemia over the period from January 1, 1962, through December 31, 1965. Positive blood cultures obtained prior to death and recorded in the files of the bacteriology department of this hospital were assembled and the corresponding clinical charts reviewed. Some records of patients with positive blood cultures were not obtainable due to improper identification, misplaced records, etc., so that the study does not represent the total experience for the stated period. The patients were predominantly white males ranging from 22 to 92 years and included two Negroes and two females. The average age was 59 years. The yearly distribution of cases over the time period is shown in Table 1. Blood cultures were performed by a closed technique using Trypticase soy broth media.† Fifteen to 20 ml. of venous blood were collected in two vacuum bottles, one anaerobically and the other with aseptically filtered air. All cultures were incubated for a minimum of five days and for a longer period, extending to 21 days, if clinically indicated. After 48 hours all cultures were subcultured on blood agar. The incidence of

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contamination has been less than 0.5 per cent.

Results

The number of organisms isolated each year is shown in Table 2.

Most Frequent Organism

There was a persistently high incidence of coagulase-positive staphylococci and *Escherichia coli* throughout the four-year period (Tables 2 and 3). In 1965 *Candida* accounted for 11.9 per cent of all isolates, but only for 4.6 per cent of the total number during the four-year period (Tables 2 and 3). *E. coli*, *Proteus* and *Klebsiella enterobacter* were the most common gram-negative organisms during the entire period (Table 3).

Source of Infection

Table 4 reveals a difference in source of infection between fatal and non-fatal bacter-

emias. The *urinary tract* was the most common source in non-fatal bacteremias, followed by the *respiratory tract*; whereas the reverse was true for fatal bacteremias.

Discussion

The preceding data show a significant increase in yeast septicemia. Nine of 10 cases occurred in the last year of the review, 1965. During the four-year span, *E. coli* and coagulase-positive staphylococci were the most common pathogens; however, in 1965 the incidence of *D. pneumoniae* was the highest. Malignancies accounted for 37.7 per cent of the underlying diseases in fatal cases and for 28 per cent in those surviving the bacteremia. Lymphomas and leukemias accounted for 35 per cent of the malignant processes in the fatal cases and for 17.9 per cent in those surviving. It is well known that patients with granulocytic leukemia have a poor leukocytic response to infection, and lymphatic leukemia is often associated with immune globulin deficiency.⁷ These factors greatly influence the course of any bacterial infection. Gastrointestinal and biliary tract disease was present in 14 of 53 patients who succumbed to their bacteremia (26.4%) and in 22 of 132 patients who survived (16.6%). Bacterial endocarditis was slightly more than twice as common

TABLE 1
Incidence of Bacteremia and Fungemia at
Minneapolis Veterans Hospital in a
Four-year Period

1962	23
1963	48
1964	52
1965	62
TOTAL	185

TABLE 2
Organisms Isolated from Blood Cultures Each Year

ORGANISM ISOLATED	1962		1963		1964		1965	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
<i>E. Coli</i>	6	25	10	19.2	8	15.0	5	7.5
Coag. Pos. Staph.	6	25	7	13.4	13	24.5	12	17.5
<i>Klebsiella-Enterobacter</i>	3	12.5	2	3.9	7	13.2	4	5.9
Coag. Neg. Staph.	3	12.5	1	1.9			1	1.5
β hemolytic Strep.	2	8.3	3	5.7	5	9.4	5	7.5
<i>Pseudomonas</i>	2	8.3	3	5.7	3	5.6	1	1.5
<i>D. Pneumonia</i>	1	4.1	6	11.5	2	3.8	13	19.6
Paracolon Group	1	4.1	3	5.7	1	1.9	5	7.5
<i>Proteus</i>			9	17.3	5	9.4	4	5.9
α -hemol. Strep.			6	11.5	3	5.6	2	2.4
γ -hemol. Strep.			1	1.9	2	3.8	5	7.5
Mimeia Species			1	1.9				
<i>C. Perfringens</i>			1	1.9				
<i>C. Albicans</i>					1	1.9	5	7.5
Group D. Strep.					1	1.9		
<i>C. Tropicalis</i>							3	4.4
Yeast (unident)							1	1.5
<i>S. Litchfield</i>							1	1.5

in fatal (7.5%) than nonfatal cases (3%). The most common source of infection for all bacteremias was the urinary tract (56 patients or 30.8%). Genitourinary tract disease was more prevalent in those surviving their bacteremia: 23 of 132 patients (17.4%) as compared to seven of 53 patients (13.2%) with fatal cases. *Proteus* was a common urinary pathogen in this study, yet it caused only two deaths in a total of 18 bacteremias. Coagulase-positive staphylococci and gram-negative organisms appear to be the major agents of bacteremia.^{1,2,4} Together they accounted for 121 of 196 isolates or 61.6 per cent. Of this total, gram-negative organisms accounted for 42.3 per cent and staphylococci 19.3 per cent. *E. coli* was the most common gram-negative isolate (34.9%). Finland et al.² compared bacteremia at Boston City Hospital in the pre-antibiotic era with the years following introduction of penicillin and broad-spectrum antibiotics. Prior to antibiotics, the pneumococcus was the most frequent pathogen. Hemolytic streptococci declined following the introduction of sulfonamides and penicillin, but the

incidence of Group D streptococci increased and persisted. The incidence of *Staphylococcus aureus* increased four-fold from 1935 to 1957, constituting the most significant increase. The pertinent findings of the present study concern bacteremias due to staphylococci and gram-negative rods as well as the emergence of another type of blood stream infection: *Candida* septicemia. These three groups of bacteremia merit a more detailed discussion.

Staphylococci Infections

Fourteen of 38 patients (37.5%) died sub-

TABLE 4
Source of Infection

Fatal Bacteremias		Nonfatal Bacteremias	
1. Respiratory tract	14	1. Urinary tract	45
2. Urinary tract	11	2. Respiratory tract	26
3. G.I.-biliary tract	10	3. Skin	16
4. Skin	6	4. G.I.-biliary tract	8
5. Unknown	11	5. Unknown	37
6. Aortic valve prosthesis	1		
Total	53	Total	132

TABLE 3
Total Number of Isolates During the Four-year Period with Percentile Distribution of Organisms and Patient Fatalities

	No. of isolates	Percent	No. of deaths	Percent of fatalities for each organism
1. β Hemolytic Coag. Pos. Staph.	38	19.3	14	37.5
2. <i>E. coli</i>	29	14.7	6	20.6
3. <i>Diplococcus pneumoniae</i>	22	11.2	3	13.6
4. <i>Proteus</i>	18	9.1	2	11.1
5. <i>Klebsiella-Enterobacter</i>	16	8.1	6	37.6
6. β Hemolytic Strep. (3 anaerobes)	16	8.1	3	18.7
7. α <i>Streptococcus</i>	10	5.1	1	10.0
8. <i>Paracolon</i>	10	5.1	3	30.0
9. <i>Pseudomonas</i>	9	4.5	8	88.8
10. γ <i>Streptococcus</i> (1 anaerobe)	8	4.1	0	0
11. <i>Candida albicans</i>	6	3.1	4	66.6
12. Staph. Coag. Neg.	5	2.5	2	40.0
13. <i>Candida Tropicalis</i>	3	1.5	0	0
14. Group D Strep. (1 anaerobe)	1	0.5	0	0
15. <i>Salmonella Litchfield</i>	1	0.5	0	0
16. <i>Clostridium Perfringens</i>	1	0.5	0	0
17. <i>Mimeis species</i>	1	0.5	0	0
18. Yeast (unidentified)	1	0.5	0	0
19. Gram-negative Rod	1	0.5	1	—
Total	196		53	

11 patients cultured 2 different organisms.

Total percent of patients dying subsequent to bacteremia = 27.

Note that coagulase-positive staphylococci represented slightly more than nineteen percent of the total number of isolates and had a mortality of 37.5. The single salmonella bacteremia is not included in the gram-negative bacteremias.

sequent to a coagulase-positive staphylococcal bacteremia. One half of the fatal cases had malignant diseases and slightly more than half had acquired the infection while in the hospital. Table 5 reveals some of the circumstances which influenced survival following staphylococcal septicemia. The five cases of coagulase-negative staphylococcal septicemia will not be dealt with here except to note that the two fatal ones had underlying aortic valve disease.

The lack of consistency in antibiotic therapy complicates the interpretation of the causes of mortality. Waisbren⁸ reports an over-all mortality of 64 per cent in 100 cases of staphylococcal septicemia, Smith and Vickers⁹ 71 per cent, Hassal and Roundtree¹⁰ 58 per cent, Allen et al.¹¹ only 27 per cent. This concerned a group of 22 cases which were treated with methicillin. Kucers and Bennett¹² report 36 per cent mortality in 33 patients in whom chloramphenicol and penicillin were the initial basic treatment. Penicillin and chloramphenicol also formed the initial therapy of the majority of patients in this study and was associated with a mortality of 37.5 per cent. In view of the increasing resistance of staphylococci to chloramphenicol, this regimen does not appear to be preferable. Methicillin and some of the newer semisynthetic penicillins have a narrow range of activity, and relatively large doses are needed for penicillin-sensitive strains.

Prophylactic Administration of Antibiotics

The prophylactic administration of antibiotics or combinations of antibiotics frequently results in infections and bacteremias due to organisms which are highly resistant to therapy.^{13,14} In this study, 11 of 38 patients received antibiotics prior to emergence of staphylococcal bacteremia; in the five fatal cases the antibiotics used were either penicillin or chloramphenicol alone or combined.

There has been a growing awareness of increased numbers of hospital-acquired staphylococcal infections.^{1,15} In this study, the initial infection of eight of the 14 fatal cases of staphylococcal bacteremia occurred within the hospital. Extremes of age, debilitating illnesses such as diabetes mellitus, malignancy, hypersensitivity diseases and skin disease have been noted to predispose patients to staphylococcal septicemia.^{8-10,12,15,16} Seven of the 14 fatal cases in this study had a malignancy and two others had diabetes. Rogers¹ study supports the impression that antibiotics have not dramatically altered the risk of infection in seriously ill hospitalized patients. He notes that 93 per cent of all bacteremias arising in the period of 1957-59 occurred in patients with serious underlying disease, whereas only 40 per cent were seen in similar patients in the era of 1938-1940.

Portal of Entry

The most common portal of entry for *Staphylococcus* has been the skin.^{8,17,18} This accounted for slightly over 18 per cent or seven of 38 patients in this review as compared with 22 per cent in Waisbren's series. A high incidence of staphylococcal infections occurs postoperatively. Cluff and associates¹⁸ noted that wound infections account for 70 per cent of acquired staphylococcal disease, the majority after laparotomy. In this study five of 38 or 13 per cent of the patients had a bacteremia following postoperative wound infections. Staphylococcal septicemia followed the use of polyethylene intravenous catheters in 12 of 86 of Hassal's patients.¹⁶ A single case has been reported previously from this hospital;¹⁹ 13 others, where an intravenous polyethylene catheter was the probable source of invasion, are also contained in this group of 196 bacteremias. In this study the respiratory tract

TABLE 5
Bacteremia Due to Coagulase-positive Staphylococci

Fatal Cases	Percent	Survivors	Percent
1. Antibiotics prior to bacteremia	5/14 35.7	6/24 25	
2. Acquired in hospital	8/14 57.1	8/24 33.3	
3. Malignancies	7/14 50	2/24 8.3	
4. Chemotherapy, steroids, x-ray	5/14 35.7	2/24 8.3	

was a source of staphylococcal sepsis equal to the skin.

In general, severe staphylococcal infection and bacteremia correlate with increasing age and debility, increased and protracted use of intravenous therapy, emergence of resistant strains of staphylococci under inadequate antibiotic cover, and use of corticosteroids, antimetabolites and alkylating agents.

Gram-negative Rod Infections

The significance of gram-negative bacteremias is obvious since they represented 42.3 per cent (83 isolates) of 196 isolates. McCabe and Jackson found a five-fold increase over an eight-year period (1951-1958). Finland and associates² observed a marked increase in gram-negative bacilli between 1935 and 1957. *E. coli* increased significantly following the introduction of antibiotics. There was a partial decrease in incidence after 1947, about the time broad-spectrum antibiotics came into general use. *Proteus* closely followed *E. coli* along with *Enterobacter* and *Pseudomonas aeruginosa*. At this hospital, *E. coli* represented 34.9 per cent of all gram-negative bacteremias, followed by *Proteus* 21.5, *Klebsiella-enterobacter* 19.2, *Paracolon* 12 and *P. aeruginosa* 10.8 per cent. A high fatality rate was seen for bacteremias of *P. aeruginosa* (88.8%) and *Klebsiella-enterobacter* (37.6%). McCabe and Jackson⁵ found a 69-per cent fatality rate with *P. aeruginosa* and mixed infections. Their study showed a significant difference between the two sexes in regard to age. More than half were seen in male patients over the age of 50, while in females one half the cases occurred below the age of 50. There was only

one woman in this group of gram-negative bacteremias; the average age of males was 65.

Malignant Disease

Eleven of 26 deaths occurred in patients with underlying malignant disease. Three had chronic lymphatic leukemia, one lymphosarcoma and one pancytopenia. Thus, five of 11 malignancies involved the hematopoietic system, again emphasizing its importance in infection.

Table 6 summarizes the mortality, the most frequent source of bacteremia, the organism most frequently responsible and the incidence of hypotension in this study and compares it to three other reviews of gram-negative bacteremia.

Genitourinary

The urinary tract was the source in 40 of 83 gram-negative bacteremias (48.1%). In 13 instances it followed a procedure involving the genitourinary tract, i.e., cystoscopy, transurethral resection of the prostate, suprapubic prostatectomy, dilatation of urethra or plastic procedures of the bladder. The frequent occurrence of gram-negative bacteremia following genitourinary tract surgery and catheterization has been recognized by others²⁰⁻²⁴; it occurs in 20 to 54 per cent of reported cases.^{22,23,25} *Proteus* and *E. coli* were the agents, each in five patients. Bacteremia followed cystoscopy in five instances and transurethral resection of the prostate in three. The gastrointestinal-biliary tract was the source of infection in 11 instances (13.2%) and the respiratory tract in seven cases (8.4%).

TABLE 6
Gram-negative Bacteremia as it Appeared in Four Independent Studies

Authors	No. of Patients	Percent Mortality	Most Frequent Organism		Incidence of Hypotension	Source of Bacteremia
McCabe-Jackson	173	42	<i>E. coli</i>	28 %	37 %	Urinary Tr. 49%
			<i>Aerobacter</i>	28 %		
Martin, W. J.	303	27	<i>E. coli</i>		20 %	Urinary Tr. 50%
Hodgin-Sanford	100	45	<i>E. coli</i>	32 %	38 %	Urinary Tr. 39%
MVAH*	83	31.3	<i>E. coli</i>	34.9%	35.5%	Urinary Tr. 48.1%

*MVAH = Minneapolis Veterans Administration Hospital

In Martin's²⁰ review of 303 gram-negative bacteremias the urinary tract was the source in about 50 per cent, the gastrointestinal tract in 15 per cent and the biliary tract in 10 per cent. Respiratory tract infection with *P. aeruginosa* was increased. In the present review, *P. aeruginosa* bacteremia in four of nine patients had the source of infection in the respiratory tract. Twenty-nine patients had a drop in blood pressure of 90/60 mm. or lower during the course of their gram-negative bacteremia. Table 7 gives the incidence and death rate for each organism.

TABLE 7
Incidence of Hypotension in Gram-negative Bacteremia

	No. of Patients	Percent	Deaths	Percent
1. <i>Klebsiella-enterobacter</i>	7/16	43	5	71.4
2. <i>Proteus</i>	7/18	39	1	14
3. <i>Pseudomonas</i>	7/9	77	7	100
4. <i>E. coli</i>	5/29	17.2	1	20
5. <i>Paracolon</i>	3/10	30	3	100
Total	29/82		17	

Shock

Shock occurred in slightly over 35 per cent of patients. More than half of the episodes (58.6%) resulted in the death of the individual. In Hodgkin's and Sanford's²¹ series shock occurred in 38 per cent with a mortality of 74 per cent. Forty per cent survived where the systolic pressure did not fall below 80 mm.; below this level, only 11 per cent of the stricken individuals survived. In this study, hypotensive episodes in *E. coli* or *Proteus* bacteremia had a much more favorable course than in pseudomonas, paracolon or enterobacter bacteremia. In general, hypotension in the former group was of shorter duration, and the response to therapy was more prompt than in the latter.

Multiple Antibiotics

Table 8 lists 19 patients who received antibiotics within a week of the bacteremia. It also lists the underlying disease, organism cultured,

antibiotic sensitivities by standard disc method, occurrence of hypotension, treatment following culture and outcome.

Thirteen of the patients had been receiving multiple antibiotics and two were also given adrenocortical steroids prior to the onset of bacteremia. Severe chronic underlying disease was present in the majority of patients (four with malignancies, three with diabetes, three with ulcerative colitis and two with Laennec's cirrhosis). Mixed cultures were found in patient No. 3, and patient No. 8 had two different organisms cultured, separated by 20-day intervals. Patient No. 12 entered the hospital as a transfer from private care and had received antibiotics unknown to the staff of this hospital prior to entry. This patient experienced two episodes of *Enterobacter* septicemia with moderate hypotension during the second episode. Patient No. 19 had chronic myelogenous* leukemia and pyelonephritis. He suffered two episodes of *Proteus* septicemia separated by a four-month interval and had received multiple, apparently appropriate, antibiotics prior to both. Patients 16, 17, and 18 experienced septicemia with highly resistant strains of *P. aeruginosa* while receiving multiple antibiotics. Petersdorf et al.²⁶ have noted that pseudomonas septicemia is likely to follow antibiotic administration.

Stamey²⁷ has stressed urine concentrations of an antibiotic as a measure of adequate therapy of urinary tract infection. He found that sterilization of the urine, as well as ultimate cure, was directly dependent on bactericidal urine level of the antibiotic, independent of the concentration in serum or plasma. Since gram-negative bacteremia so often originates from the urinary tract, this becomes an important factor. However, Ronald et al.²⁸ contend that agents which attain high antibacterial concentrations only in the urine should not be used in treatment of patients suspected of having renal parenchymal involvement. He notes that patients with chronic bacteriuria who relapse with the same strain usually have infection in the kidney, whereas reinfection with new strains is more common in patients with bladder bacteriuria. When relapses with the same strain occur, a successful course of therapy can be attained with antibiotics having bactericidal

*See Test Your Word Score Page 1513.

TABLE 8
Nineteen Patients Who Received Antibiotic Therapy Within One Week
Prior to the Onset of Bacteremia

Patient	Underlying Disease	Blood Culture	Bacterial Antibiotic Sensitivity	Prior Antibiotics	Hypotension	Treatment After Culture	Outcome
1. TD 68 M	Acute cholecystitis	E. coli	R-Pen., Eryth.	Tetr.	No	Cholecystostomy, Chloro.	Survived
2. EC 70 M	Pulm. toc., Ca. lung, UTI	E. coli	R-Pen., Eryth. S-Chloro., Tetr.	Pen.	No	Chloro.-responded	Died 20 days after pos. cult. of meta-static Ca.
3. PTK 75 M	Diab. mell., Pneumonia, UTI	Proteus E. coli	R-Chloro., Strep. (only) S-Neo. (only)	Pen.	75/40	Hypotension not sustained. Aramine, Chloro., Strep., Steroids	Survived
4. AEJ 67 F	Chronic pyelonephritis	E. coli	R-Pen. S-all others	Gantrisin	No	Tetr., Chloro.	Survived
5. FBG 46 M	Laennec's cirrhosis, Bilat. pneum.	E. coli	R-Pen. S-all others	Pen. Chloro.	No	Tetr.	Survived
6. HFS 69 M	Diab. mell., Arthritis, Pyelonephritis	E. coli	R-Pen. S-Strep., Tetr., Chloro.	Tetr., Steroids	No	Chloro., Nalidixic acid	Survived
7. GAH M	ASO-gangrene BPH-obstructive	Paracolon	R-all tested except S-Novo.	Pen. Chloro.	No	Expired 12 hr. after admission. Continued Pen., Chloro.	Died of bacteremia
8. RJT 53 M	Malig. teratoma testes, ASO-gangrene	Proteus 9/5/63 Paracolon 9/25/63	R-all tested S-Neo. (only) R-all tested S-Neo. (only)	None Pen., Tetr., Chloro.	No No	Pen., Tetr., Chloro. I.V. Tetr., Pen.	Survived Died of bacteremia
9. LHT 71 M	Acute cystitis acute prostatitis	Paracolon	R-Pen. S-Chloro.	Tetr., Nitrofur.	No	Chloro., Nitrofur.	Survived
10. KAB 49 M	Laennec's cirrhosis, perf. sigm. divertic	Paracolon	R-Pen. S-all others	Tetr.	No	Surgical drainage, Eryth.	Survived
11. HH 76 M	Choledocholithiasis, UTI	Paracolon	R-Pen. S-Chloro., Strep.	Oxytetracycline	Slight	Oxytetracycline	Survived
12. FS 55 M	RHD, AS, AI	Enterobacteria Enterobacteria	S-Tetr., Neo. (only) R-Pen. (only) S-all others	Unknown Antibiotic Strep., Chloro.	No Mod. hypo.	Chloro., Strep., Tetr. Tetr.	Survived Survived
13. ALG 61 M	Ulcer. colitis, perforated	Enterobacteria	Not tested	Naf., Pen., Steroids	64/0	Tetr., Steroids, surgery	Died of bacteremia
14. FEK 66 M	Ca. pancreas, subdiaphragmatic abscess	Enterobacteria	R-Pen. S-all others	Pen., Naf.	86/48	Tetr., Keflin	Died of bacteremia
15. WSK 71 M	Ulcerative colitis; diabetes mellitus	Enterobacteria	Not tested	Pen., Chloro.	80/40	Pen., Chloro., I.V.	Died of G.I. bleeding

Continued

TABLE 8 (Continued)

16. JDF 74 M	Head injury, UTI	Pseudo- monas	R-all except S-Poly B	Eryth., Strep., Pen.	65/0	Chloro., Pen., Steroids, vasopressors	Died of bacteremia
Patient	Underlying Disease	Blood Culture	Bacterial Antibiotic Sensitivity	Prior Antibiotics	Hypotension	Treatment After Culture	Outcome
17. FH 69 M	Traumatic rectal perforation	Pseudo- monas	R-all except S-Nitrofur.	Chloro., Pen.	74/5	Surgical drain, Coly- mycin	Died of bacteremia
18. FW 69 M	Ulcerative colitis; bronchitis	Pseudo- monas	R-all except S-Poly B, Strep.	Chloro., Keflin, Eryth.	60/0	Keflin, Chloro., Steroids	Died of bacteremia
19. CM 70 M	Chronic ML and chronic pyelonephritis	Proteus	R-Pen.	Colymycin,	No	Keflin, Strep.	Survived
		Proteus	S-all others R-Pen., Tetr. S-all others	Tetr., Nitrofur., Mand.	Slight	Keflin, Gantrisin, Nitrofur.	Survived
	AI		Aortic insufficiency.	RHD		Rheumatic heart disease.	
	AS		Aortic stenosis.	S		Sensitive.	
	ASO		Arterioscler- osis	Strep		Streptomycin.	
			obliterans.	Tetr		Tetracycline.	
	BPH		Benign prostatic hypertrophy.	UTI		Urinary tract infection.	
	Chloro		Chloram- phenicol.				
	Chronic ML		Chronic myelogenous leukemia.				
	Eryth		Erythromycin.				
	Mand		Mandelamine.				
	Naf		Nafcillin.				
	Neo		Neomycin.				
	Nitrofur		Nitrofur- an- toin.				
	Novo		Novobiocin.				
	Pen		Penicillin.				
	Poly B		Polymyxin B.				
	R		Resistant.				

levels in both blood and urine, such as ampicillin.

Candida Septicemia

Candida albicans was established as the etiologic agent of thrush in 1846. Later, Virchow showed that it was capable of deeper penetration, after he found it in the submucosa of the esophagus.²⁹ It was once believed to be the only pathogenic member of the genus, but Schurtleff,³⁰ Richart and Dammin³¹ have found *Candida tropicalis* capable of producing disseminated disease as well. This species causes disease indistinguishable from that caused by *C. albicans*. In this study, six

cases of *C. albicans* septicemia, three *C. tropicalis* and one unidentified yeast were cultured from the blood of 10 patients. In four the *Candida* was either directly responsible or a major contributory factor to the demise of the patient. In two others, it may have been a contributing factor. Table 9 summarizes the age, sex, underlying disease, organism, antibiotics used prior to the fungemia, clinical and in some cases autopsy findings.

Five patients had a neoplasm and three were diabetics. Patients 1-4 were thought to have died as a result of the *Candida* sepsis. Nine of the 10 received broad-spectrum antibiotics prior to or during the septicemia. Eight received

chloromycetin and seven penicillin; none were treated with Amphotericin B. Five patients developed signs of renal failure and four hypotension.

Hematopoietic Disease

It has been emphasized that patients with

disseminated fungal infections often are suffering of a primary hematopoietic* disease such as leukemia, lymphoma, aplastic anemia and related leukopenic disorders, or are receiving steroids, alkylating agents or antimetabolites as well as broad spectrum antibiotics.³²⁻³⁴ In this study, all five neoplasms occurred in the

TABLE 9
Candida Septicemia
Patients With Fatal Candida Septicemia

Patient	Primary Disease	Blood Culture	Prior Antibiotics	Clinical Course	Autopsy Findings	Autopsy Culture
1. FW 71 M	Chronic pyelonephritis	Candida albicans	Chloro.	Progressive oliguria, fever, hypotension.	Focal abscesses of kidneys, adrenals, heart, lungs	Candida albicans
2. HH 69 M	Obstructive duod. ulcer, diabetes	Candida albicans	Pen., Naf., Chloro.	Fever, oliguria, hypotension 6 days postop. partial gastrectomy	No autopsy	
3. SL 68 M	Pyelonephritis, diab. mellitus	Candida albicans	Naf., Chloro., Amp.	Fever, progressive renal failure	Focal abscesses of heart, spleen, lung, kidneys	Candida albicans
4. GD 53 M	Cholecystitis, ASO	Candida albicans	Pen., Chloro.	High fever (105°), uremia, hypotension	Gangrenous gall bladder	
Other Patients With Significant Candida Septicemia						
5. CM 78 M	Ca of rectum	Candida tropicalis	None	Fever in terminal stage of illness, hypotension	Metastatic carcinoma	
6. EP 75 M	Ca of colon	Candida albicans	Chloro., Eryth.	Fever, terminal oliguria, hypotension, peritonitis	Metastatic carcinoma of colon	
7. CB 69 M	Ca of esophagus	Candida albicans	Pen., Chloro.	Fever, sudden cyanosis, hypotension	Carcinoma of esophagus, pulmonary infarct	
8. IT 52 M	Ca of sigmoid colon	Candida tropicalis	Pen., Chloro.	Fever only; spontaneous remission following discontinuance of antibiotics	Survived	
9. EEP 42 M	Acute ulcerative colitis	Yeast	Pen., Naf.	Fever only; spontaneous remission following discontinuance of antibiotics	Survived	
10. AK 59 M	Ca of pancreas, diabetes mellitus	Candida tropicalis	Pen., Oxacillin, Chloro.	Wound infection, oral moniliasis, fever.	Metast. carcinoma of the pancreas	

*See Test Your Word Score Page 1513.

gastrointestinal tract; three other patients had non-malignant disease of this system, and none received steroids, alkylating agents or anti-metabolites prior to the *Candida* septicemia.

Suppressing Bowel Flora

Harrell,³⁵ Braude and Rock³⁶ noted that acute disseminated candidiasis frequently develops against a background of continuous antibiotic therapy during the course of a protracted debilitating disease, particularly when normal bowel flora is suppressed. In experiments, certain broad-spectrum antibiotics (tetracycline and aureomycin) have been shown to enhance the virulence of *C. albicans*.³⁷ In a review of 48 cases of disseminated candidiasis, Hurley²⁹ noted that antibiotics had been given in 43; however, there was also a history of serious underlying disease. She concludes that antibiotic therapy cannot be the sole predisposing factor to fatal moniliasis since the incidence of fatal fungus infections has not increased since the introduction of antibiotics in England where her study was performed. But Seelig⁶ and Zimmerman³³ in this country claim an increased incidence. The present study would tend to support them as well as the claim that serious primary disease is invariably present.

Tissue Damage

The gastrointestinal tract has been stressed as a source of systemic candidiasis.^{6,31,36} Braude and Rock³⁶ noted that mucosal injury in patients on antibiotics was the usual setting for the dissemination of *Candida*. Eleven cases of 31, reported by Louria,³⁸ had severe pharyngeal or gastrointestinal lesions which led to dissemination. This was the likely source in four of our patients. Another source is provided by protracted intravenous therapy, especially with use of a polyethylene catheter. Case No. 4 had a well documented focus on the tip of the indwelling catheter from which *C. albicans* was cultured. A similar set of circumstances was suspected in three others.

Renal insufficiency during the course of systemic candidiasis has been encountered experi-

mentally and clinically. Richart and Dammin³¹ described two cases of disseminated *C. Tropicalis* which resulted in renal failure and central nervous systemic depression. The organism was found most often in the yeast phase in early tubular lesions. Hyphae* were noted to form in the periphery of lesions of experimental infections. Little inflammatory response was found at autopsy unless tissue necrosis had been produced.

Shock following intravenous injection of *Candida* has been produced in dogs;³⁹ it was more profound with intact cells than with disrupted cells and supernatant. Three patients in this study, Nos. 1, 2, and 4, had definite evidence of endotoxin-like shock manifested by oliguria, hypotension, fever, mental disturbances and progressive renal failure.

None of these ten patients received specific antifungal therapy. The problem of treatment with Amphotericin B is often compounded by the presence of compromised renal function. The effectiveness of Amphotericin B has been demonstrated by Louria et al.,⁴⁰ but prolonged high plasma concentrations are necessary. The prophylactic use of antifungal antibiotics, such as Nystatin with antibacterial agents, has been shown to be effective in reducing the candidal counts in the stools, although less effective in reducing the overgrowth in sputum.³⁰ Seelig⁶ points out that this is not unusual since direct contact of the antifungal agent with the *Candida* is necessary for antifungal activity. Increased awareness of the seriousness of the problem may prompt early intervention. The prophylactic use of oral antifungal agents might be considered for debilitated patients who are receiving prolonged antibacterial therapy.

Conclusion

Bacteremias with coagulase-positive staphylococci and gram-negative bacteria produced the majority of deaths in this study and were often superimposed on a background of neoplastic disease, especially of the hematopoietic system. Other chronic debilitating diseases of major significance in fatal cases are diabetes mellitus, gastrointestinal-biliary tract disease and chronic lung disease. In non-fatal bactere-

*See Test Your Word Score Page 1513.

mia, genitourinary tract disease was a common underlying condition and source of infection. An increasingly more frequent portal of entry is the intravenous polyethylene catheter. Shock during the course of bacteremia was associated with a mortality of almost 60 per cent. *P. aeruginosa* and *C. albicans* were found to complicate malignant disease, produce shock and follow antibiotic therapy in a high percentage of patients harboring these pathogens. The high death rate of *Candida* septicemia in this study bears emphasis and occurred in patients

with non-malignant disease of the gastrointestinal or biliary tract and with diabetes mellitus. Five of 10 patients suffering *Candida* septicemia had a malignant lesion; however, these patients survived the sepsis. Progressive deterioration in renal function and mental status and hypotension were manifested by all patients dying from yeast septicemia and should be considered an indication for more vigorous therapy. There has been a striking increase in the incidence of *Candida* septicemia within the last two years.

References

1. Rogers, D. E.: Changing Pattern of Life Threatening Microbial Disease. *New Eng J Med* 261:677, 1959.
2. Finland, M., Jones, W. F. and Barnes, M. W.: Occurrence of Serious Bacterial Infections Since Introduction of Antibacterial Agents. *JAMA* 170: 2188, 1959.
3. Maiztegui, J. I., Biegeleisen, J. Z., Cherry, W. B. and Kass E. M.: Bacteremia Due to Gram-Negative Rods. *New Eng J Med* 272:222, 1965.
4. Yow, E. M.: Clinical Significance of Rising Incidence of Infections Due to Gram-Negative Bacilli. *Postgrad Med* 17:413, 1955.
5. McCabe, W. R. and Jackson, G. G.: Gram-Negative Bacteremia. *Arch Intern Med* 110:847, 1962.
6. Seelig, M. S.: The Role of Antibiotics in Pathogenesis of *Candida* Infections. *Amer J Med* 40: 887, 1966.
7. McHenry, M. C., Martin, W. J., Hargraves, M. M. and Bagenstoss, A. H.: Bacteremia in Patients with Neoplastic or Hematologic Disease. *Proc Mayo Clin* 37:43, 1962.
8. Waisbren, B. A. and Abboud, F.: Bacteremias Due to Coagulase-Positive *Staphylococcus*. *Ann Intern Med* 52:643, 1960.
9. Smith, I. M. and Vickers, B. A.: Natural History of *Staphylococcal* Septicemia. *Lancet* 1:1318, 1960.
10. Hassal, J. E. and Roundtree, P. M.: *Staphylococcal* Septicemia. *Lancet* 1:213, 1959.
11. Allen, J. D., Roberts, C. E. and Kirby, W. M. M.: *Staphylococcal* Septicemia Treated with Methicillin. *New Eng J Med* 266:111, 1962.
12. Kucers, A. and Bennett, N.: *Staphylococcal* Septicemia. *Med J Aust* Feb. 25, 1964.
13. Bauer, A. W., Perry, D. M. and Kirby, W. M. M.: Drug Usage and Antibiotic Susceptibility of *Staphylococci*. *JAMA* 173:475, 1960.
14. Bernstein, C. A. and McDermott, W.: Increased Transmissibility of *Staphylococci* to Patients Receiving Antimicrobial Drugs. *New Eng J Med* 262:637, 1960.
15. Minchew, B. and Cluff, L.: Studies of Epidemiology of *Staphylococcal* Infection. *J Chron Dis* 13:354, 1961.
- 16-40 May be secured from the author or the reprints.

How To Mount

My first ambulance call was set for the evening of June 30th, and they made it a transfer of a patient from Beth Israel Hospital up to Bellevue Hospital. I telephoned my family that I had received my first orders, and was ready in my uniform with the ambulance bag in my hand when Dick Bateman who was the driver on duty backed the ambulance in. He quickly jumped down and ran around to me saying: "Doc, I want to show you a trick or two, how to get on the bus, if you want me to." Did I want him to! Good, kind Dick Bateman; in a five-minute demonstration he showed me just what and what *not* to do, and I have been eternally grateful to him. He showed me how to sit on the seat and with one quick bounce swing both feet up from the step of the ambulance over the tailboard and so into the "bus." He made me rehearse this three or four times and I soon found it was not unlike mounting a horse. When once you were on the seat, a sense of balance helped you to keep it and there were two solid leather hand straps that I gratefully relied on at first. I have always felt that this careful, thoughtful instruction gave me a good start and as soon as I had the proper technique, I never knew what physical fear was in our roughest and hardest driving.*

*Emily Barringer, M.D.: *Memoirs of a Lady Ambulance Surgeon*, Bowery to Bellevue, 1950.

Mr. President—Your Health***James Madison (1751-1836)**

Our fourth President, James Madison, belonged in that category of medical paradoxes whose longevity belies their constitutional frailty.

Though never robust as a child, young James enjoyed outdoorsmanship; he rode horseback and hiked in the woods and fields, observing birds in particular. Communion with nature, however, did not preclude a predilection for study, which took him through a four-year college course at Princeton in slightly over two years.

During his teens and early twenties Madison complained of voice impairment, a functional handicap that prevented his public speaking until he was 30. Correlative with his vocal weakness was "a constitutional liability to sudden attacks of the nature of epilepsy," doubtless hysteric rather than neurogenic in origin, but which undermined his morale and prevented his demonstrating his inherent ability.

Because he was shy and sensitive Madison's own assessment of his constitutional stamina was low, if not depreciatory. Despite his good fortune in escaping such prevalent diseases as malaria, tuberculosis, smallpox, and yellow fever, he was neurotically convinced that his body harbored some insidious malady, an obsession he finally overcame only with prodigious determination.

Physically Madison was always frail in appearance, short of stature, and slight—never weighing over 100 pounds to his five feet, four to six inches. With age his complexion became sallow and his eyes blepharitic. Though unimpressive physically, he was withal ever a gentleman of good breeding and a patriot of statesmanlike dimensions.

From his middle years on, Madison was plagued with biliousness and arthritis, for neither of which medical science offered much relief. Of his disabilities his wife once wrote to a friend:

"My dear Husband is still confined to his bed. In addition to a disabling rheumatism throughout the winter, he has had a bilious fever, which has reduced him so much that he can only walk from one bed to another. I never leave him more than a few moments at a time, and have not left the enclosure around our house for the last eight months on account of his continued indisposition, concerning which friends at a distance have rec'd but too favourable reports. Our Physicians have advised the Warm Springs for Mr. Madison, and we hoped to have taken him there, but as he could not travel unless conveyed on his bed, we dare not think of it at present."

Had Madison lived in the twentieth instead of the eighteenth century gall-bladder surgery and sulfa drugs might have relieved his chronic cholecystitis and progressive arthritis. However, it was not until he reached his early eighties that arteriosclerotic deterioration set in, impairing both his vision and his hearing. He just began to fade away, growing thinner and weaker until one morning he was found dead in his bedroom sitting in front of his untouched breakfast tray.

In spite of the numerous functional ailments of his earlier life and the organic pathologies of his later years Madison had reached the august age of 85 years, three months, and 12 days.

*With acknowledgments to Karl C. Wold, M.D.: Mr. President—How Is Your Health?

Tell me to what you pay attention and I will tell you who you are.—Ortega Y Gasset

Alcoholism

The problems of modern medicine are creating moral, scientific, and ethical implications which medicine and theology must consider. They must develop for society certain guidelines by which modern medicine can move into these new areas.

The first of these is that of the ethical implications on organ transplant. It is more than the laboratory's technical skill and procedure which can be either successful or not successful in the taking of an organ from a living being and transplanting it into another living being. It involves many ethical questions and decisions which must be discussed, because each patient is a patient unto himself, and the families create circumstances which make us approach patients in different attitudes of mind. Joseph E. Murray, M.D.*, has said in "The Unrelated Donor:"

"Justification even for the use of a cadaveric kidney or a 'free' kidney is not automatic just because the prospective recipient is otherwise doomed to die. . . . All the more difficult to justify is the use of living volunteer donors. Although chemical suppressive agents may be effective temporarily, many questions remain unanswered. . . . 'The potential dehumanizing abuses of a market in human flesh' is a phrase used by Lederberg (in MAN AND HIS FUTURE). Although admitting that his attitude may be construed as an 'alarming or ungracious reaction to the gift of life,' he warns against misguided medical progress in the name of humanity. Physicians removing intact organs from healthy donors without a conscientious concern for the problem of better procurement may be likened to the old lumber barons felling trees indiscriminately. . . . To our knowledge no healthy living donor has yet been an operative fatality, yet fatal operative complications are always possible. As physicians motivated and educated to make sick people well we make a basic qualitative shift in our aims when we risk the health of a well person, no matter how pure our motives. To relieve ourselves of this responsibility we must strive for better organ procurement so that the day will come when even identical twins will not require a living donor."

We are dealing not only with the kidney, for I know the day will come through research, understanding, and knowledge in medical science when we will be in the position to transplant all types of human organs, as well as install plastic and artificial ones. Recently at a College of Surgeons Meeting, a physician, speaking on the work which is being done concerning the plastic heart, called attention to the idea that within three or five years it was going to be possible to place a plastic heart inside the patient, replacing his present damaged heart. The question that might then be asked from a moral, ethical implication is: what is life?

In our modern-day society we consider that death prevails when the heart ceases to beat. Oft times we go to extreme measures or artificial and mechanical ways to keep the heart beating. The patient appears alive; though in any reasonable sense of mentality, ability to move, to love, or to receive love, he no longer exists. When the time comes that we are able to place a plastic heart inside the chest cavity of the individual, then the question might need be asked: when does this patient's life cease? Theologically it is an age-old question—what is life? But with the advances of modern medicine, these are areas where only the theologian and the physician can honestly give guidelines to society. Perhaps we are going to need other ways of measuring life and death.

"The bioelectric activity of the living brain is silenced by anoxia which soon produces cerebral death. Respirators and heart stimulators can maintain the look of life in the face of death while agonizing and expensive prolongation of false hope continues for all concerned. When the brain is so comprised, the EEG can signal the point of no return, although the

Continued

*Assistant Clinical Professor of Surgery at Harvard Medical School.

cardiovascular system continues to respond to supportive therapy that produces a respectable ECG. Supportive efforts should be continued only so long as the brain shares physiological response together with heart and lungs. Adequate experience has been analyzed to show that competent application and interpretation of the EEG should gain medical approval for legal pronouncement of human death."*

There are no easy answers. We must confront ourselves as physicians and as theologians in dialogue and in communication, in consultation, in agreement and in disagreement, for we are not dealing with ourselves; we are dealing with our patients and our parishioners who are whole persons.

The two professions of medicine and religion must become deeply concerned with the life and the total health—of every individual. From their collective judgment will come the means for providing the most effective care and treatment of the patient as a whole man. This is the new concept. The two forces, medicine and religion, with one goal—knowing full well that illness may be organic, may be spiritual, may be emotional, or may be social—must solve the dilemma. This, then, is our one goal—total care.

*Hannibal Hamlin, M.D.: "Life or Death by EEG" JAMA, October 12, 1964.

President's Letter

(Continued from page 1459).

rug! My wife understands. She has had holes in ours too, plus about everything else in the house: card tables, night stands, kitchen table, you know, the usual places! I've got a tremendously expert dry cleaner. He has someone who works for him who can fix those holes in my pants so that you can hardly see them—the cigarette holes, I mean.

I don't believe a word of that cancer guff! Those companies who offer coupons with their packs of cigs should really offer pneumonectomies for 2,000 coupons. That should really encourage people to smoke their brand! And guarantee cures too! One thousand more for the cobalt!

When you get close to tobacco-addicted patients, your nose doesn't readily detect their telltale odor, if you yourself are a smoker. But if you're not one, no patient can conceal his

odoriferous vice from you. Now that I don't smoke any more, I realize how charitable my patients had to be toward me: a first-class stinker, until I swore off. Besides, your office girl may be allergic to the stuff but really hate to say anything. After all, she likes to work for you otherwise—good pay . . . , but cigars!!! Bury the dead!!

I'm just getting wound up, but the editor wants me to stop. There is a limit, you know. Happy smoking, colleagues!!



C. G. Sheppard, M.D.

President

Minnesota State Medical Association

Man is a wonderful fellow, learning from the other animals the way he does. He studies the hawk and the vulture and flies through the air with the greatest of ease. He learns from the crab with its shell and the skunk with its tear gas. He considers the ways of the squirrel and becomes a hoarder; the ways of the snake in the grass and the shark and the crocodile, the mole and the hedgehog, and makes himself terrible on land and sea and underneath both. . . . About the only creature left in nature for him to learn something useful from is the dove.

New York Times Magazine



Editorials

Nodular Lesions of the Leg

ALTHOUGH THERE may be no specific "Nodule of the Leg" syndrome, the condition is common enough to be a challenge to many disciplines of medicine. For the female adult population with the overexposure that their lower extremities must endure, disfiguring nodules are disturbing, and care is mandatory for cosmetic reasons if for no other. The majority of patients with this condition ultimately find their way into the office of the dermatologist. Most of these conditions are only part of a generalized dermatological disease; but because of involvement of the leg where their presence is more obvious and therefore more unsightly, there is greater concern on the part of the patient.

Aside from the dermatological problems such as lichen planus,* psoriasis and localized dermatoses, there are many leg nodules that are of significance as monitors of systemic illness. Erythema nodosum certainly must be the most significant of the painful type of leg nodules. Their relationship to tuberculosis and beta hemolytic streptococcus disease has been known for many years. However, more recently we have learned of their presence in association with such less well known entities as histoplasmosis, coccidioidomycoses, sarcoidosis and psittacosis, to mention only a few. Erythema nodosum may also be seen with some drug reactions such as bromides, iodides and sul-

fanilamides. Erythema multiforme with its varied types and presentations is a less frequent cause of inflammatory leg nodules but may be present in many of the situations that are associated with erythema nodosum. Weber-Christian syndrome as one of the causes of inflammatory leg nodules is of more recent description, as well as the nodular fat necrosis of acute pancreatitis. These and other causes of leg nodules are described in the July issue of MINNESOTA MEDICINE by Dr. Carl Laymon.**

Pulmonary osteoarthropathy as the monitor of certain lung conditions can present as erythematous nodular lesions of lower legs and feet. Localized myxedema is a relatively rare complication of Graves' disease and is seen in some patients with severe exophthalmos. This condition usually occurs in the outer portion of the lower third of the legs and presents as a non-pitting, painless swelling which may have a purplish, reddish color. Necrobiosis diabetorum is manifested by firm, yellowish plaques present usually on the anterior surface of the lower leg.

Recognition of urticaria, thromboses of varicosities and insect bites are no great problem. However, when multi-hued nodules, indurated or soft, small or large, discrete or diffuse, bilateral or unilateral, present themselves, dermatological consultation is sought in many instances. The dermatologist can often point to a systemic etiology and provide the needed tip to solve a perplexing diagnostic problem.

John W. Johnson, M.D.
Minneapolis, Minnesota

*See Test Your Word Score Page 1513.

**Laymon, Carl W.: Nodular Disorders of the Legs. Minnesota Med. 50:1059, 1967.



DUAL PROBLEM IN PEPTIC ULCER

Relief of hyperacidity is still a primary goal in the treatment of peptic ulcer. And antacids are the most widely used means of achieving this relief. But antacids alone cannot influence the distention and bloating which so often add to ulcer distress.

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Food Allergy

ALLERGY to foods has been observed for many centuries. The real incidence of food allergy is unknown, but that it is common cannot be denied. Perhaps the majority of persons have at one time or another had occasional or mild complaints referable to a specific food, usually infrequently eaten and easily detected. In such conditions as gastrointestinal complaints, headaches, urticaria, asthma, rhinitis, insufficient importance is given to food allergy.

Age is a factor bearing on the incidence and possibility of food allergy. In infants, foods are common allergens. In adults, although other types of allergens seem more important, foods still play a role in allergic manifestations. In asthma or rhinitis food will frequently be an additive factor to the inhalants as a cause of symptoms. Removing the offending foods may give relief even though other allergens are also involved, and vice versa. Hyposensitization to these other allergens may allow the patient to eat the same foods with impunity.

Almost any food may produce allergy, but if one were to name a limited list of foods commonly mentioned as allergens these would include egg, wheat, milk, peas, beans, nuts, fish, onions, white potato, chocolate and some fruits.

The antigens responsible for allergic symptoms after ingestion have not been subjected to as much study as the inhalants. Allergy to cows' milk has been studied extensively. Milk is a complex liquid containing at least sixteen antigens identifiable on immunoelectrophoresis with rabbit antiserum to milk.¹ Despite some claims that heat-treated milk causes fewer symptoms than unheated milk in allergic individuals, a recent study showed that heated milk is capable of provoking symptoms in milk-allergic children.² It therefore appears that heat-resistant antigens, alpha lactalbumin, beta lactoglobulin and casein are of great interest. Goldman studied the importance of these antigens and bovine serum albumin in milk-sensitive children. He found that in milk allergy four different allergens are implicated about equally, and that the pattern varies from person to person.² Egg-sensitive individuals are usually sensitive only to the egg white, and skin reactions can usually be elicited with purified egg

albumin as well as with whole egg white. The other proteins of egg white have not been studied for antigenicity in man. Careful evaluation of individual antigens by provocative tests has not been done in other food allergies.³

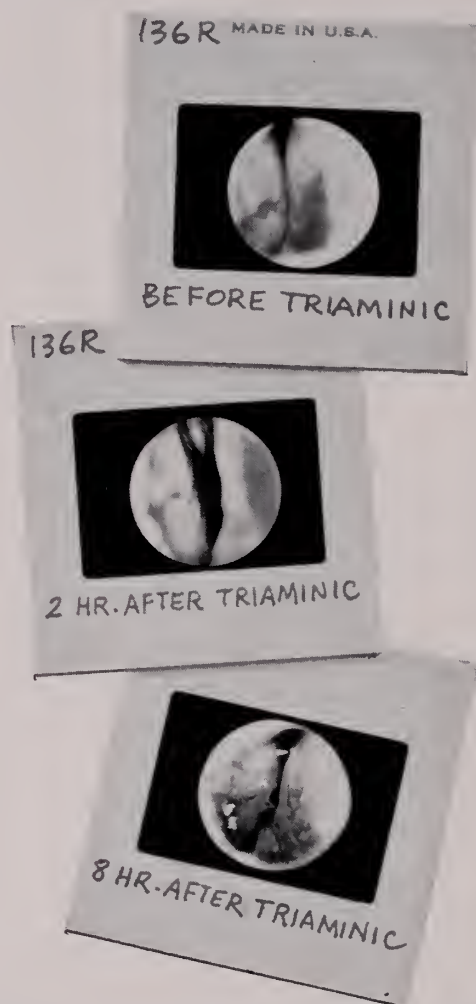
The importance of the foods seems to vary with the allergic complaints. Thus fish and strawberries frequently cause urticaria, while cocoa and nuts are often involved in migraine. Urticaria frequently follows the eating of fish, shellfish, nuts or fruits. Positive skin reactions and the presence of passive transfer antibodies are more common here than in food allergy associated with other symptoms. The allergens involved have not been identified except in urticaria due to oranges, in which cholorogenic acid seems to be the allergic determinant.³

With common food, it is very difficult to detect the culprit, as any food may cause practically any manifestation. The resulting symptoms may become manifest within a few minutes to several hours after ingestion and may last many days. Furthermore, foods may contain substances, such as antibiotics, which may act as antigens. While ingestion is, of course, the usual mode of contact, it should be remembered that injections, inhalation and direct contact are also possible avenues of exposure. For instance, the miller and the housewife are exposed to inhalation of wheat, and food odors contain sufficient allergens to result in trouble. Another factor is the state of the food, as well as the quantity. A person may not have difficulty with small amounts of a food, while large amounts of the same food may result in symptoms. Some foods, according to many allergists, may be tolerated when cooked or baked although they do provoke symptoms when raw. While it is a common belief that allergic people may have allergy to foods they dislike, in the majority of cases no such allergy exists.

The diagnosis of food allergy is not accurately or even easily made by any method to date. Much confusion has resulted in recent years, especially since skin testing to foods and provocative tests from the injection of foods have frequently resulted in confusion due to too great expectation and too little supervision and cooperation. Too often other factors have been disregarded: in-

Continued

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halants, psychic trauma, drugs, and infection. Many times the patient is given a list of skin tests and told he is "allergic" to the positive tests, not realizing that a positive skin test may or may not mean present sensitivity. Also, even though the history and provocative tests suggest food allergy, reactions to skin tests with the foods are often negative. The frequent appearance of precipitating antibodies to food antigens in the serum have not been diagnostically helpful in general. They are frequently present in individuals who are not food-sensitive.⁴ Furthermore the antigen which is absorbed from the intestine has been partially digested and may therefore be altered to a new antigenic specificity.

Although various methods for the detection of food allergy and therefore treatment have been suggested, dietary manipulation is still the most practical. It is based upon controlling the symptoms by diet and then adding foods which, if responsible, will produce clinical effects. Rotation diets, basic diets with additions, dietary methods, diets based on skin tests, and diets based on common allergic foods have been used.

Food allergies are prevalent in the United States, especially with the increased variety of foods on the market. Unfortunately, food allergy is a diagnosis frequently mentioned, occasionally studied correctly, and rarely established. It deserves more evaluation.

Malcolm N. Blumenthal, M.D.*
Minneapolis, Minnesota

*Department of Internal Medicine, University of Minnesota.

References

1. Hanson, L. A., and Maussion, I.: Immune Electrophoretic Studies of Bovine Milk and Milk Products. *Acta Paediat* (Stockholm) 50:484, 1961.
2. Goldman, A. S., Anderson, D. W., Jr., Sellers, W. A., Saperstein, S., Kniker, W. T., Halpern, S. R., et al.: Milk Allergy: I. Oral Challenge with Milk and Isolated Milk Proteins in Allergic Children. *Pediatrics* 32:425, 1963.
3. Norman, P. S.: Antigenes that Cause Atopic Disease, *Immunological Diseases*. Max Samter, Editor, Little Brown and Company, Boston, pp. 511.
4. Saperstein, S., Anderson, D. W., Jr., Goldman, M. S., and Kniker, W. T.: Milk Allergy: III. Immunological Studies with Sera from Allergic and Normal Children. *Pediatrics* 32:580, 1963.

The Assessment of Vertigo*

A DIFFICULT problem in the assessment of vertigo from the clinician's standpoint is to get an adequate description of the patient's symptoms. People mean many different things by the term "dizziness," and patients who have nonorganic disturbances in the sense of balance seem to have much more trouble describing their symptoms than do those who have actual organic lesions such as acoustic neuroma or Meniere's disease. If a patient has true Meniere's disease, usually little difficulty is encountered in getting a description of rotary vertigo together with nausea and vomiting and the usual fluctuating loss of hearing with tinnitus in the involved ear. The caloric test or electronystagmogram may show any results from normal function to complete canal paresis. The audiologic tests are much more

valuable in making the diagnosis. In patients who have acoustic neuromas, however, the response to caloric stimulation is always reduced or possibly absent. In a large group of patients whose histories indicate episodes of true rotary vertigo, all audiologic and vestibular tests show normal results, and the neurologist is unable to find any evidence of disease of the central nervous system. In my opinion, a diagnosis of Meniere's disease should not be made in these cases until the audiologic examination reveals evidence of sensori-neural hearing loss in one ear. Much remains to be learned about the function of the vestibular apparatus and of the cochlea. The advent of a practical form of cortical audiometry may assist greatly in animal experimentation to determine the cause and the treatment of Meniere's disease and its associated conditions.

James B. McBean, M.D.
Rochester, Minnesota

*McNally, W. J.: The Assessment of Vertigo. *Minnesota Med* 50:1003, 1967.

Learn to Doubt

Seeking to know is only too often learning to doubt.—Antoinette Deshoulières

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*Based on Statistical Report, U.S. Dept. Commerce, ed. 86, and Fisher, G. F., and Vavra, H. M.: Pub. Health Rep. 80:961 (Nov.) 1965.

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Special Management Problems in Diabetes

AS OUTLINED by Kirtley in the March* issue of MINNESOTA MEDICINE, the management of stable diabetes is relatively uncomplicated. Variations in insulin dosage usually depend on fluctuations in glycosuria, ketonuria, fasting and postprandial blood sugar levels, and the time of occurrence and frequency of hypoglycemic reactions. Such variations are by definition minimal in stable patients, and the timing of the insulin injection, meals, and exercise poses no particular problem in management.

It is the special problems posed by pregnancy, excessive lability, insulin resistance, and lipotrophic diabetes which tax the diabetologist's resourcefulness. The majority of pregnant diabetic patients have a rise in insulin requirement during the second and third trimesters of pregnancy;¹ and a rise in plasma levels of insulin occurs also in the third trimester of normal pregnancy.² This increase in insulin needs during pregnancy may be due to placental lactogen,^{3,4} in which case decreases in insulin requirement in the last trimester in diabetic pregnancy may indicate fetal death or portend neonatal complications.

In order to attain adequate control in the pregnant diabetic, the insulin dosage should be adjusted as frequently as required by variation in the different measures of the diabetic state so that the extremes of hyperglycemia with ketoacidosis and of hypoglycemia, which may be detrimental to both mother and fetus, are avoided. Rigid adherence to set doses of insulin or to a set program of insulin management may result in ketoacidosis or hypoglycemia. The need for marked reduction of insulin dosage on the day of delivery to avert catastrophic hypoglycemia has been urged¹ and should be well known. It is best to reduce the insulin dose to one fourth the usual dose or to none at all on the day of delivery. Continuous intravenous administration of glucose solution may be necessary to avoid severe hypoglycemia during the first 24 hours post partum. Insulin dosage can be subsequently gauged by determinations of glucose in the blood and urine.

Patients usually return to the pregestational needs for insulin within the first week.¹

Excessively unstable diabetes mellitus requires diligent consideration. This condition has been defined as a "syndrome of excessively variable insulin sensitivity and ketosis-proneness manifested by extreme and unexplainable short-term and long-term fluctuations in the parameters of the disease."⁵ These patients may be clinically characterized by total insulin deficiency, variable sensitivity to insulin, and excessive proneness to ketosis and leanness.⁶ Fortunately they do not comprise a large percentage of the diabetic population, but they present a most challenging problem. The best program for these patients from the standpoint of diabetic control is multiple doses of soluble crystalline insulin given before a standard feeding every six hours.^{6,7} This program lessens the swing of the pendulum of hyperglycemia-hypoglycemia. As one modifies this program of multiple doses of soluble insulin to one of varied combinations of unmodified and modified insulin in one or more doses daily, the safety zone for predictable insulin effect has been crossed. The latter fact needs particular emphasis in consideration of the proper insulin program for any patient with excessively unstable diabetes mellitus.

Bolinger and colleagues⁸ have submitted data from disappearance rates for radioiodinated insulin to support the view that unstable diabetes in some patients is best controlled by a single daily morning injection of insulin with proportionately larger amounts of soluble crystalline insulin than of the modified long-acting preparations of insulin. Williams and colleagues⁹ have also demonstrated a sustained action of regular insulin in some juvenile-onset diabetics. It may be, therefore, that patients with excessively unstable diabetes may do worse with multiple doses of modified insulin preparations. Nowhere in diabetic management is it more important to tailor the management program to the individual patient than in excessively labile diabetes mellitus.

The treatment of insulin resistance will be dictated by the cause. In acromegaly, Cush-

*Kirtley, W. R.: Insulin Preparations. *Minnesota Med* 50:315, 1967.



"All Registered Nurses are Alike"

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ing's disease, malignant neoplasia, and infections, the treatment is obvious: remove the cause and the insulin hyporesponsiveness is ameliorated. However, chronic insulin resistance with the need for 200 or more units of insulin daily with elevation of insulin antibodies in the serum is best treated with porcine insulin, especially when higher levels of antibodies to bovine than to porcine insulin can be demonstrated.¹⁰ Treatment with desalinated porcine insulin,¹¹ human insulin,¹¹ and sulfated insulin,¹² as well as treatment with adrenal steroids¹⁰ and with combinations of the oral antidiabetic agents with insulin,¹³ has also been tried with beneficial effect.

An interesting variety of insulin resistance has been described in association with acanthosis nigricans* in two patients in whom end-organ failure or cellular hyporesponsiveness was apparently involved.^{14,15}

We have recently had the opportunity of evaluating a 14-year-old girl with acanthosis nigricans, who had had diabetes for approximately one year. She had no diabetic complications. Regardless of whether she received 1,000 or more units of insulin or no insulin at all, her blood sugar levels and quantitative values for urinary glucose remained essentially unchanged. She showed no tendency to develop ketoacidosis. There was no evidence of other endocrine disease. Values for blood cortisols and urinary 17-ketosteroids and ketogenic steroids were within normal limits. Her insulin antibody levels were in the usual range for stable uncomplicated diabetes (8.7% by the Skom-Talmage method). Pharmacologic doses of adrenal steroids did not ameliorate the insulin resistance but, in fact, exacerbated the diabetes with increasing hyperglycemia. Phenformin alone and in combination with insulin had little effect. A trial with porcine insulin was not undertaken. Her condition as of the last follow-up (at 18 months) remained unchanged.

Generalizations regarding the outcome in this special group of patients with insulin-resistant diabetes secondary to cellular hypo-

responsiveness cannot be made because clinical experience with such patients has been limited to a few cases. The patient of Tucker and colleagues¹⁵ died with nephropathy and cerebellar infarction; the patient of Field and colleagues¹⁴ survived with spontaneous remission of the insulin resistance in 18 months.

Lipoatrophic diabetes is another form of insulin-resistant diabetes mellitus. It is characterized by complete absence of subcutaneous, intra-abdominal, and perinephric fat with onset usually in the teens or occasionally later, little tendency for ketoacidosis to develop, hepatosplenomegaly, hyperlipemia with cutaneous xanthomata, and marked hypermetabolism without hyperthyroidism.¹⁶ Because of the cellular hyporesponsiveness in these patients, the quantity of insulin administered apparently makes little difference; however, one should strive for optimal control with the use of insulin or a combination of oral antidiabetic agents, or both. Clinical experience with this group of diabetic patients has also been limited to a small number of cases.

Distinct from this group of patients with lipoatrophic diabetes is a larger group with lipoatrophy secondary to insulin therapy. These patients may have mildly elevated insulin antibody levels (approximately 30% binding by the Skom-Talmage method), yet insulin requirement is low (less than 40 units of insulin daily) relative to the antibody titer. We have observed that some of these patients have benefited by the use of porcine insulin; the areas of lipoatrophy have filled in, the insulin antibodies have decreased over a one-year period, but the insulin requirement has not changed appreciably.

Hence pregnancy, excessive lability, insulin resistance of whatever cause, and lipoatrophic diabetes present special management problems in diabetes mellitus and, although every program of diabetic management needs to be individualized, these special problems make tailoring of the diabetic program to the individual patient of paramount importance in treatment.

Pasquale J. Palumbo, M.D.
Rochester, Minnesota

*See Test Your Word Score Page 1513.

References may be secured from the author or the reprints.

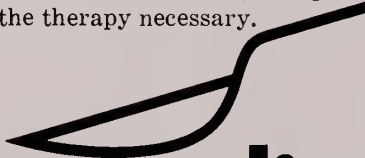
Read over your composition, and whenever you meet with a passage you think is particularly fine, strike it out!—Dr. Samuel Johnson (quoting his tutor)



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Anatomic Lymphatic-Venous Connections Demonstrated by Lymphangiography

PRESSMAN AND BURTZ* have emphasized that it is possible for tumor cells or bacteria to pass from lymph nodes directly into the bloodstream. This fact should be taken into account in order to form an accurate concept of the role of lymphatics in the dissemination of cancer and infection.

Another lymphatic anatomic consideration that may have great bearing on the spread of cancer or infection by lymphatics is the presence of anastomoses between lymphatic vessels and adjacent veins. Lymphangiography

has dramatically demonstrated that these anatomic connections are functional. During lymphangiography, the contrast medium (Ethiodol) occasionally can be seen with image intensification fluoroscopy and spot roentgenograms to enter these direct connections from lymphatic vessels to veins. If lymphatic obstruction is present, large amounts of Ethiodol may be seen to enter veins via these communications. It seems likely, therefore, that cancer or infection which disseminates via the lymphatics may spread tumor cells or bacteria directly into the bloodstream by these lymphatic-venous anastomoses.

*Pressman, J. L., and Burtz, Mildred V.: The Anatomy of the Lymphatics: Relationship to the Dissemination of Malignancies and Infections. *Minnesota Med.* 50:789, 1967.

W. Eugene Miller, M.D.
Rochester, Minnesota

Test Your Word Score

Pyrrole—*a colorless liquid obtained from the distillation of animal substances: C_4H_5N ; smelling like chloroform and turning a reddish hue when treated with certain acids* (page 1463).

Hypertrichosis—*abnormal growth of hair* (page 1464).

Adiadochokinesia—*inability to perform rapid alternating movements* (page 1467).

Anamnestic—*pertaining to anamnesis: the process by which antibodies which had disappeared from the blood are redeveloped by injection of an antigen* (page 1471).

Ototoxic drug—*having toxic action upon the ear* (page 1472).

Myelogenous—*produced in the bone marrow* (page 1494).

Hematopoietic—*pertaining to formation of blood cells* (page 1497).

Hyphae—*fungus filaments* (page 1498).

Lichen planus—*an inflammatory skin disease with wide flat papules* (page 1503).

Acanthosis nigricans—*hyperpigmentation and roughness of the skin* (page 1511).

Pyroninophilic—*characterized by increased affinity for pyronine: seen in plasma and reticuloendothelial cells prior to the development of amyloidosis* (page 1524).

Anhidrosis—*abnormal deficiency of sweat* (page 1544).

Syringomyelia—*a condition marked by abnormal cavities filled with liquid in the substance of the spinal cord* (page 1544).

Tetralogy of Fallot—*a triad of congenital malformations in the heart with hypertrophy of the right ventricle* (page 1545).

Macrophage—*large "wandering cell" originating in the tissues* (page 1567).

Cylindruria—*the presence of tube casts in the urine* (page 1572).

Achlorhydric—*characterized by absence of hydrochloric acid from the gastric secretions* (page 1576).

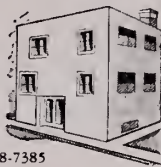
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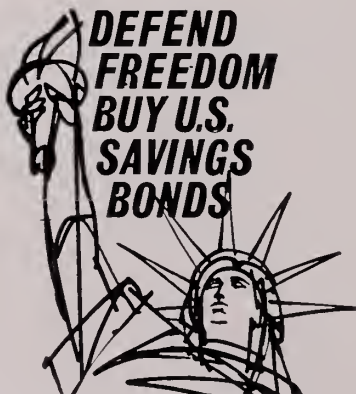
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You May Be Right

In regard to the report on porphyria by Shuman and Snively*, I should like to mention a case in which a diagnosis of myocardial infarction was made and later proven to be porphyria.

This was a case of a farmer who developed acute chest pain while he was in a boat out fishing. The electrocardiogram was interpreted as showing a myocardial infarction. About five days following the so-called infarction he developed abdominal pain, which was considered to be a mesentery embolism. The question was whether or not he should be explored.

When I saw the patient it was my opinion that the electrocardiogram showed, instead of an infarction, pericarditis. There was probably some involvement of the muscle underlying the pericardium, but the primary change did not show the reciprocal changes that one would expect with a true infarction. Because the patient was so extremely ill, one would not say that this was an epicardial infarction. Therefore, we sought another cause for the chest pain followed by abdominal pain, and we were fortunate enough to prove the diagnosis of porphyria.

Following his recovery the patient has had very little difficulty if he stays out of the sun and away from barbiturates.

We have had several cases of porphyria with cutaneous manifestations and hepatic involvement. These can be very mild when the patient knows what to avoid, and particularly if we treat the acute episode with ACTH.

Owen L. Slaughter, M.D.
Evansville, Indiana

*See page 1463.

Pathiatry

This particular cult is trade-marked. "It combines the best principles of spinal adjustment, traction, manipulation, deep massage, etc., administered by oneself. So simple and delightful as to become a part of the daily toilet. Done anywhere, at any time, while standing, even sitting; without appliance of any kind."

—Morris Fishbein, M.D.: *The New Medical Follies*, 1927.

The mind's direction is more important than its progress.—Joubert

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The Editor's Soliloquy

The Veto

To express an honest difference of opinion is justifiable and commendable. But some individuals are so constitutionally perverse—so contra-suggestive—so fractious—that they feel impelled to present an alternative to your every utterance; not only to every personal opinion you express, but even to every factual statement you make. They become an adversary, as it were. In their judgment you are misguided, uninformed, deluded—or even wilfully wrong. If they can't actually contradict what you say, they feel bound to at least qualify it. If not prepared to take vital issue with you, the caviller may be prone to demand finer distinctions and greater specificity in your choice of words.

If such a quibbler happens to be a neighbor and you greet him with "It looks like rain," he will veto your observation by citing a falling barometer reading. If you counter by saying that you detected a touch of mist in the air, he will cite too low a humidity reading for moisture to be noticeable.

If you comment on the exhilaration of winter, you are reminded that summer requires no snow shovelling; if you express a predilection for the balminess of summer, you are reminded that the rigors of winter kill off the bugs.

Such a person may have been your host and you thank him on your departure for a pleasant evening. He will question your sincerity and, if you glower, will speculate on your biliary function.

Should he be a colleague with whom you are discussing a case and you suggest a diagnosis of protein deficiency, he may counter with kwashiorkor; if you speculate on a middle-ear infection, you are apt to be bowled over with Guillain-Barre syndrome. What you call progeria, calcinosis, and nocturnal hemoglobinuria become in his exalted vocabulary Hutchinson-Gilford disease, Thibierge-Weissenbach syndrome, and Marchiafava-Micheli.

The contra-suggestive individual is indigenous to all areas and social classes. He has no identifying marks to alert you in advance that you are meeting up with an antagonist. Perhaps, after a futile and frustrating hour or so in his company, you decide that you will surely be invulnerable if you embark on some such irrefutable and sacrosanct subject as God, Motherhood, or Country. But you are mistaken, for he responds to the challenge with flagrant cases of atheism and heresy; illegitimacy and the unidentified orphan on the doorstep; or the enormous provocation for the Founding Fathers to turn over in their graves.

Carl O. Rice, M.D.

"I'll speak to thee in silence."—Shakespeare-Cymbeline

Old Doc Hess says: There are two kinds of "psychogenic" disorders: (1) those for which the doctor easily learns the psychic cause; and (2) those for which the doctor fails to find the organic cause.—C.O.R.

Most ignorance is vincible ignorance. We don't know because we don't want to know.—Aldous Huxley

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Curbstone Consultation

QUESTION: A 44-year-old man has a history of a six-week visual loss in the left eye at age 25; since then he has had a three-week episode of paresthesia involving the entire right upper limb, and another ten-day episode of diplopia recently. Except for bilateral extensor plantar responses, absent abdominal reflexes, and a pale optic disc on the left side, there are no other findings. Examination of the cerebrospinal fluid shows 53 mg. protein, 10 lymphocytes, a gamma globulin concentration of 26 per cent (upper limit of 13 per cent) but no other changes. How specific for multiple sclerosis is the finding of an increased concentration of gamma globulin in the cerebrospinal fluid after protein electrophoresis?

ANSWER: The elevation of gamma globulin in the cerebrospinal fluid is not specific for any disease of the central nervous system, and this finding must be interpreted with knowledge of the entire clinical picture. Seventy per cent of patients with multiple sclerosis will have this change, and the patient described almost certainly has this disease.

But similar elevations may be encountered in neurosyphilis (e.g., tabes dorsalis), in acute viral encephalitis, in fungus meningitis, in some brain tumors, and in diseases with elevation of the serum gamma globulin. Cerebrospinal fluid gamma globulin concentration is characteristically elevated in patients with the uncommon inflammatory disease, subacute inclusion body encephalitis.

Allan J. D. Dale, M.D.
Rochester, Minnesota

QUESTION: A 50-year-old diabetic male has progressive gangrene of the toes of the right foot. In addition, there is rest pain in the foot and lower leg. Otherwise the patient shows no evidence of severe vascular disease, and the diabetes is easily controlled with insulin. A sympathectomy was performed three years ago with some symptomatic improvement. A recent femoral arteriogram reveals complete occlusion of the superficial femoral and popliteal arteries. The anterior tibial artery is patent in the mid-calf. The pain is so severe that the man wishes his leg amputated. Is there any reconstructive procedure currently available to attempt to revascularize this leg?

ANSWER: Recent technical advances in the manufacture of suture material and needles make surgery for relatively small blood vessels feasible. Femoral-anterior tibial arterial reconstruction, utilizing autogenous saphenous vein, should be considered in cases of this type. A number of patients have been relieved of pain and have been spared amputation by this reconstruction. It should be borne in mind, however, that surgery of this type is palliative and does not prevent the progression of atherosclerosis.

Theodore A. Peterson, M.D.
Minneapolis, Minnesota

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The Viewing Box

Cardiac Enlargement in Uremia

THE PATIENT was a 24-year-old white male with a history of chronic glomerulonephritis who received a homograph renal transplant in June, 1965. Due to a chronic rejection phase, the patient had the transplanted kidney removed in June, 1966 and has been anephric since. His course on hemodialysis has been essentially stable with good control of his uremia. In July, 1967, due to occasional anterior chest pain, a roentgenogram of the thorax was obtained and showed an enlarged cardiac silhouette (Figure 1). The patient was hospitalized for evaluation.

Two days after admission a pericardial friction rub was noted, that persisted for about 2-3 weeks. His rhythm was generally sinus, with bouts of atrial flutter. A radioisotope scan of the cardiac blood pool was done using iodine 131-labelled human serum albumin (RISA) (Figure 2).



Figure 1

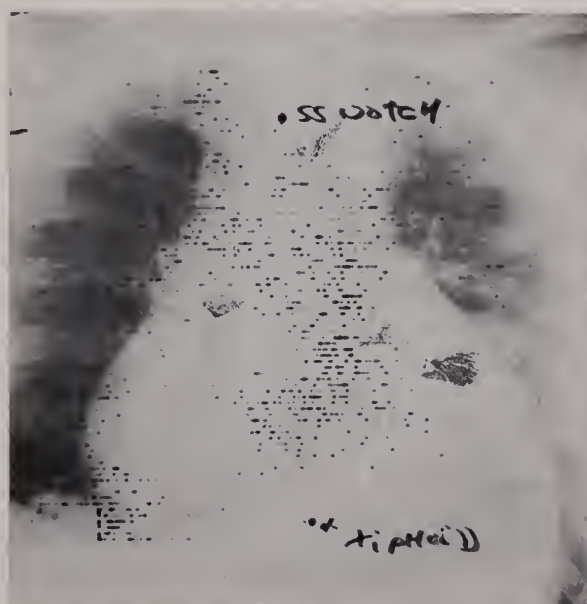


Figure 2

What is your diagnosis? (See next page).

Diagnosis. Uremic pericarditis with effusion.

In Figure 2 the scan is superimposed upon the roentgenogram. It shows a small cardiac blood pool within a large cardiac silhouette, indicating the presence of a massive pericardial effusion.

Pericarditis is defined as inflammation of the enveloping membranes of the heart, i.e., the visceral or parietal pericardium, or both. Pericarditis may be the sole cardiac lesion but is more commonly seen in association with myocarditis, endocarditis, or both.

Pericarditis seems to be a relatively common complication of uremia. Before the era of dialysis, its presence was regarded as a sign of impending death. With renal transplantation and dialysis being more widely used, the following have become apparent:

- (1) Uremic pericarditis is more common than previously realized.
- (2) Uremic pericarditis may have no correlation with the clinical state of uremia.
- (3) With treatment, reports of cardiac tamponade, which was considered rare in uremia, are increasing, many with complete recovery.

The basic mechanism of the development of pericarditis in uremia is not well understood. Therapy seems to be the diligent treatment of the underlying uremia. Clinically the prognosis is less grim, and tamponade, should it occur, should be vigorously treated. Radioactive isotope scanning is a good method to confirm the presence of a pericardial effusion.

Neil Hoffman, M.D.
Department of Medicine
Hennepin County General Hospital

A Frontier Post Mortem

The Tombstone Epitaph of those days contained stories which showed why the doctor had every opportunity to become a proficient surgeon. On July 8, 1882, the paper told how Deputy Sherrill Phillips was killed while arresting a drunken Mexican who was flourishing his revolver in a saloon.

Phillips died in the saloon, and the Epitaph reported:

"A post mortem examination of the murdered man by Dr. Goodfellow, showed the nature of the wound to be as follows: The bullet entered the upper part of the right arm passing through the pectoral muscles in front of the armpit, entered the chest cavity between the first and second ribs; thence passing through the upper lobe of the right lung; thence through the upper left lobe of the lung, in the left side of which it lodged. Death occurred from hemorrhage into the windpipe and pleural cavities."*

*Richard Dunlop, M.D.: Doctors of the American Frontier.

Remedies For Fevers

Deer's flesh is a febrifuge. Periodical and recurrent fevers are cured, if we are to believe what the magicians tell us, by wearing the right eye of a wolf, salted, and attached as an amulet. There is one kind of fever generally known as "amphemerine;" it is to be cured, they say, by the patient taking three drops of blood from an ass's ear, and swallowing them in two semi-sextarii of water. Other adepts recommend for quartan fever, the salted liver of a cat that has been killed while the moon was on the wane, to be taken in wine just before the paroxysms come on.



Tumor Conference

A Liver Transplant^{*}

Dr. Walter L. Mersheimer:^{**}

Our topic this morning is liver transplantation and our first speaker is Dr. Joel Smith, resident in the Department of Surgery, who is going to discuss the history of liver transplants.

Hepatic Homotransplantation

Dr. Joel Smith:[†]

Spurred on by the success of Drs. Murray and Hume in their work with renal transplantation, Dr. C. Stuart Welch at the Albany Medical Center began his investigation into the technique and feasibility of hepatic homotransplantation. He performed auxiliary liver homotransplantations in dogs wherein the donor liver was placed into the pelvic region of the host, and its portal vein anastomosed to the distal portion of the now severed host inferior vena cava. Its own infra-hepatic inferior vena cava was ligated, and its supra-hepatic inferior vena caval cuff was then joined to the infra-renal inferior vena cava of the host. The arterial blood supply to the graft was supplied by the host aorta, without removing the host's own liver and without administering immunosuppressive therapies.

Results

Immediate function of the grafted liver was evident. Its output of bile via a cholecystostomy tube and its clearance of administered bromsulphalein were at a minimum on the third postoperative day and thence declined until the death of the host on the fifth or sixth postoperative day.

The hepatic graft's tolerance to anoxia was limited to thirty-three minutes.

Round cell invasion and mononuclear infiltration first appeared in the grafted liver on the fourth postoperative day.

Autolysis

At about the same time, Dr. Francis Moore and Dr. A. S. Sicular had been evaluating methods which could lessen the amount of autolysis and increase the critical tolerance to anoxia in the immediate post-mortem organ.² These

^{*}Presented at Surgical Conference, November 16, 1966, New York Medical College, Flower and Fifth Avenue Hospitals.

^{**}Professor and Chairman Department of Surgery, New York Medical College.

[†]Resident in Surgery, New York Medical College.

Continued

methods which included donor organ hypothermia were then employed in their series of orthotopic liver homotransplants wherein the host's liver was removed and replaced with a graft liver³. Many of these dogs survived twelve days, although as with Welch's procedures immunosuppressive drugs were not given.

Hepatic Outflow Block

Dr. Thomas Starzl and his group at Denver, Colorado, evaluated the role of hepatic anoxia in outflow block, the histologic changes in the grafted liver and other problems met with in hepatic transplantation.⁴

It had been noticed that early failures exhibited livers which were swollen, cyanotic and tense. Acute portal venous hypertension was evident. This condition was found to be caused by a block to hepatic outflow of blood by the sphincteric action of the well-developed smooth muscle layer present in the small hepatic veins. This hepatic outflow block had also been noticed in dogs suffering endotoxic, peptone and hemorrhagic shock. It was concluded that the grafted liver reacted to the transplantation anoxia with this throttling mechanism and now began to accumulate all the blood entering it until gastrointestinal infarction and hemorrhage began its deleterious attempt at decompressing this acute portal hypertension. Further attempts at hepatic transplantation had to consider reducing the amount of liver ischemia as well as perhaps reducing its supply of blood should outflow block become imminent. An extracorporeal hypothermic perfusion pump technique and various patterns of vascular anastomoses were developed to lessen these problems.

Immunosuppressive Agents

Immunosuppressive agents, notably azathioprine, were now administered to the transplant animals, and Starzl was able to prolong their survival significantly. Histologically, parenchymal destruction and perivascular inflammation was evident; however, the minor degrees of pyroninophilic* cellular invasion and monocytic invasion would lead one to conclude that these agents reduced the cellular mechanism of graft rejection.⁵ The role of the humoral factors in rejection of hepatic grafts thus became predominant, especially since Hans Popper reported the role of the hepatocyte as a target cell for antigen and antibody complexing with subsequent destruction of this cell. Sicular showed that gamma globulins can affix themselves to the hepatocytes, the blood vessels and the bile ducts of the liver graft. Other agents included Azaserine, actinomycin C, S-35 labelled methionine and, most recently, Anti-lymphocyte serum.

Starzl employed some of these agents and reported marked increases in the survival rates of grafted dogs.⁶ Twenty per cent of the dogs with hepatectomies and orthotopic liver transplants showed no clinical evidence of rejection and one third of this large series exhibited rejection that was reversible without increasing the amount or the frequency of azathioprine. A small number of the dogs were able to survive after the azathioprine was discontinued and some were reported alive well over twenty months after their transplant operation.

Of the seven reported attempts at human orthotopic liver transplants,⁷ five were done by Starzl in Colorado, one each was done by Moore and Demirleau. Six patients had primary hepatomas, the seventh, congenital biliary atresia. Two died during surgery; the others survived six to twenty-three days.

*See Test Your Word Score Page 1513.

The problems encountered included the use of severely injured and anoxic donor livers which, however, did not suffer from the detrimental complication of hepatic outflow block met with in the canine experiments. Although the livers were severely damaged, serial laboratory data showed this injury to be reversible.

Poor Clotting

The patient with a diseased liver enters the procedure with inherently poor clotting powers. During the actual transplant, acute and severe fibrinolysis compounds this problem.⁸ This phase of hypofibrinogenemia and hyperfibrinolysis is partially improved some hours after canine hepatectomy, suggesting that other organ systems can control this increased fibrinolysis in the anhepatic organism. It is also believed that on re-establishing the afferent and efferent blood supplies to the anoxic liver, fibrinolysins or their activators (which might be produced in the damaged graft) now gain access to the host circulation with detrimental results. Dr. Starzl tried to control this acute fibrinolysis in his patients by using epsilon amino caproic acid, fresh blood and fibrinogen. However, this intra-operative hemorrhagic phenomenon was soon followed postoperatively by a period of rebound hypercoagulability which was only intensified by the prior addition of clot-promoting agents.

Many patients had peripheral venous thromboses during the hypercoagulative, hyperfibrinogenemic phase which often became manifest later on as pulmonary emboli.

The histologic study of the orthotopically placed human homotransplant showed good preservation of liver function and architecture, minimal immunocyte invasion and minimal hepatocyte loss. Death was not due to liver failure or immunologic rejection. Indeed the longest survivor died of bile peritonitis secondary to a technically caused necrosis of the common bile duct.

Physiologically Favored Homotransplant

The employment of the auxiliary liver homotransplant seems advantageous in patients with medically irreversible hepatic failure wherein their own liver need not be removed at that time, if at all. Experimentally, however, it was found that in dogs having this technique and treatment with azathioprine, the grafted livers began to shrink after two weeks and continued to do so. If we recall Dr. Welch's scheme, we see that the major blood supply to the graft was furnished by the recipient's inferior vena cava. Marchioro working in Starzl's laboratory concluded that the physiologically favored liver in this auxiliary technique would be the one receiving the substrates included in the non-hepatic splanchnic venous blood flow.⁹ Should neither directly receive this important flow, the liver obtaining the greater blood flow would be the favored one. A patient's diseased liver has lost most of its capacity for this competition, and indeed this substrate dependency is lost. To facilitate a better flow of blood into the auxiliary liver graft, Starzl performed a portocaval shunt in two patients with Laennec's cirrhosis prior to the actual transplantation.¹⁰ The auxiliary livers functioned immediately but deteriorated after seven to 10 days. Nevertheless, the patients survived: one died on the 22nd day of staphylococcal pneumonia, the other on the 34th day of hemorrhagic monilial enterocolitis, cytomegalic virus inclusion disease and pneumocystis carinii infection. Active rejection of the homograft was severe only in the patient dying of pneumonia.

Continued

A third attempt at auxiliary hepatic homotransplantation was made in a 15-month-old child with biliary atresia with immediately poor results due to technical complications. Other auxiliary transplants have already been performed by Absolon, Hermann, Cree, Hume and Gliedman, the latter four not as yet reported.

TABLE
HISTORICAL EVENTS IN LIVER TRANSPLANTATION

February, 1956	First auxiliary liver homotransplants in dogs by Goodrich et al. at Albany Medical Center.
March, 1963	First clinical liver homotransplantation and first orthotopic canine liver homotransplants by Starzl et al. at Denver, Colorado.
September, 1963	Clinical orthotopic liver transplant by Moore in Boston.
January, 1964	Clinical orthotopic liver transplant by Demirleau in Paris.
November, 1964	First clinical auxiliary liver homotransplant by Absolon in Minneapolis.
February, 1965	Further clinical auxiliary liver homotransplantations by Starzl et al. in Denver, Colorado.

Case Report

Dr. Michael Antonelli:*

A 17-year-old negro male was admitted to Metropolitan Hospital on October 21, 1966, with the chief complaint of jaundice. Four days prior to admission he noted anorexia, nausea and dark urine. He later developed jaundice, experienced malaise, and had one episode of vomiting. He had not had a bowel movement for two days. There was no abdominal pain. No previous history of jaundice, dark urine or food intolerance could be obtained. He admitted to having taken two injections of heroin six weeks previously, but was not a habitual user of drugs. Past history included an umbilical herniorrhaphy in 1957. He had had pneumonia, "glandular fever", and tonsillitis as a child.

Physical Findings

Physical examination revealed a well developed, well nourished negro male in no distress: blood pressure 120/56, pulse 60, and temperature 100° F. The only positive physical findings were icterus of sclerae and mucous membranes, a grade I/VI systolic murmur at the left sternal border in the recumbent position, a liver that was barely palpable below the right costal margin, and punch tenderness over the liver. Flat plate of abdomen and chest films were negative.

Laboratory Studies

Laboratory data on admission included a bilirubin of 7.7, alkaline phosphatase of 29.5 K.A. units, albumin of 4.7, and globulin of 3.1. Sick cell prep. was negative. Hb. was 14.7 Gm., Ht. 46%, wbc. 8,500 with 25% segs., 73% lymphs and 2% eos.; platelets were 170,000, FBS 110, BUN 16 and prothrombin time 23 secs. with a control of 14.5 secs. Electrolytes were normal.

On October 24 his bilirubin was 1.8 direct—13.6 total, SGOT over 216, SGPT over 180. The patient appeared well until the night of October 24 and the morning of October 25, at which time he became markedly agitated. Physical examination showed pupils that were equal and responded to light, normal deep tendon reflexes, no pathological reflexes, and no asterixis. The liver was not palpable and by percussion appeared smaller than previously noted. He was started on Decadron, 10 mgm. I.V. Stat. and every six hours, 10% D/W, neomycin by mouth and neomycin enemas. A blood ammonia was drawn and later reported as 162 µg. %. Later in the day his coma deepened, the patient responding to painful stimuli only. His Decadron was increased to 20 mgm. every six hours intravenously.

Progress

On October 26 he was comatose, not responding to painful stimuli. His temperature had risen to 101° and râles were heard over the lung fields. His bilirubin was 7.8 direct, 20.9 total, BUN 5, prothrombin time of over 60 seconds, alkaline phosphatase of 40.3 KA units and a thymol turbidity of 11.3. A tracheostomy was performed and penicillin started intravenously. Some dark blood was obtained through a nasogastric tube and hematuria was noted.

*Resident in Medicine, New York Medical College.

At this time an exchange transfusion of 10 units of blood removed and 11 units infused was performed in 500 cc. aliquots. After transfusion his bilirubin had fallen to 16.3, his alk. phosphatase to 34 and his prothrombin time to 34 secs. with control of 14 secs. The bleeding from the tracheostomy, bladder and stomach ceased, and he was now responsive to painful stimuli with occasional spontaneous movement.

The next day, October 27, his coma was deeper again with dilated pupils. He had a respiratory and cardiac arrest while being suctioned, but regular sinus rhythm was restored within 1-2 minutes, with a blood pressure of 94/60. He required a Bird respirator for maintenance of respiration, and blood pressure had to be maintained with Isuprel and later Aramine. His blood ammonia had risen to 470 μ g.

A second exchange transfusion was performed with 13 units of fresh heparinized blood. After seven units his ammonia had fallen to 320 μ g. However, at the end of the exchange, his coma had not appreciably lightened. His body temperature fell to 94° and he was maintained on a thermal blanket, Bird respirator and vasopressors. Late that night an operation was performed.

Exchange Transfusions

Dr. William Rosenthal:*

Within the past 15 or 18 years, considerable information has been presented on the clinical course and biochemical background of hepatic coma, the complete pathogenesis of which still remains to be elucidated. On a purely empirical basis, a number of lines of therapy have been developed. Patients with hepatic encephalopathy seem to fall into two groups: those with exogenous coma and those with endogenous coma.

Exogenous Coma

In the first group the patients have something in their recent past which is responsible for the coma. Either they had some ammoniacal material such as protein, urea, etc., or they have had a drug which affects ammonia metabolism or cerebral metabolism. With removal of these materials from the diet or the therapeutic regimen, the patient usually improves.

Endogenous Coma

The second group has proven much more difficult. This includes patients with massive liver injury as seen in carbontetrachloride poisoning, acute fulminating viral hepatitis, or progressive broad deterioration of liver function as seen in the end stage of cirrhosis. In these patients the blood ammonia levels have been less well correlated with the degree of coma. Removal of potential toxic substances from their therapeutic or dietary regimen does not seem to help. It is this group in which medical results have been extremely poor to which we are addressing ourselves today. Corticosteroids have been used with some degree of success in fulminating viral hepatitis. Massive doses of corticosteroids in the hands of Katz et al.¹¹ resulted in a fall of the mortality rate from approximately 99% to around 60%. This drug has become the mainstay of medical therapy. Despite the fact that these results have been difficult to duplicate in large series, we have seen a few patients at this institution who appear to have responded to this therapy. In general, however, results have been extremely poor. Certainly the elimination of bacteria from the G.I. tract to reduce the absorption of toxins in this group has been useless. The use of dialysis will be discussed by Dr. Treser. However, in view of the failure of these efforts, a new approach has been replacement of the patient's blood with normal blood to remove the cause of the

*Associate Professor of Medicine, New York Medical College.

Continued

coma and result in improved cerebral function. Exchange transfusion¹² should be viewed as a method of "buying" time for the patient while his liver regenerates enough for survival.

Exchange Transfusion

A larger report by Trey et al.¹³ was that on seven patients from South Africa, five of whom survived as a direct result of exchange transfusion. In fact one of the patients received seven exchange transfusions and survived. Most of the patients required only one or two transfusions and the very encouraging part of this report was that each patient made dramatic response to the exchange, actually becoming far more responsive immediately after exchange transfusion. As you will recall, in our patient this did not occur. There was only a slight response to the first exchange and little or no clinical change with the second. Although these cases from the literature seem promising, some weeks later in the correspondence columns of the *NEW ENGLAND JOURNAL* the editors mentioned that one of the authors had received 11 letters from people around the world stating that they had tried exchange transfusion with failure.

Dialysis

Dr. Gerhard Treser:*

Dialysis seems to be of limited value in the treatment of hepatic coma. Many say it is of no value at all. However, we are able at least to remove ammonia at quite a fast rate and correct the pH and electrolytes. There are reports where dialysis at least achieved a temporary improvement in these patients, and we were able to reduce the ammonia from 1,000 μ gm. to 150 μ gm., with the electrolytes normal after dialysis. Our aim in this is to give the surgeon more time to prepare for the operation and to look for a suitable liver.

Dr. Mersheimer:

Thank you, Dr. Treser. I think that in introducing the next speaker I would like to state that Dr. Ian Campbell Cree joined our staff here July 1 of this year. He was trained primarily in England; then he spent a year on a Rockefeller Fellowship at the Mayo Clinic where he did exclusive research on organ and tissue transplant problems. I met him as he was completing this fellowship and tried to get him to join our staff. However, since he was here on an exchange visa, he had to leave the country for two years and went to the University of Saskatchewan where he was in the Department of Surgery and headed up their renal and liver transplant investigations.

A Liver Transplant

Dr. Ian Cree:**

Thank you, Dr. Mersheimer. It is a great honor for me to be able to work in this college. I have been tremendously impressed by the staff here and by the outstanding potential of this college. This liver transplant was in essence a last ditch attempt to save this young boy who was only 17 years of age

*Research Associate, Department of Medicine, New York Medical College.

**Associate Professor of Surgery, New York Medical College.

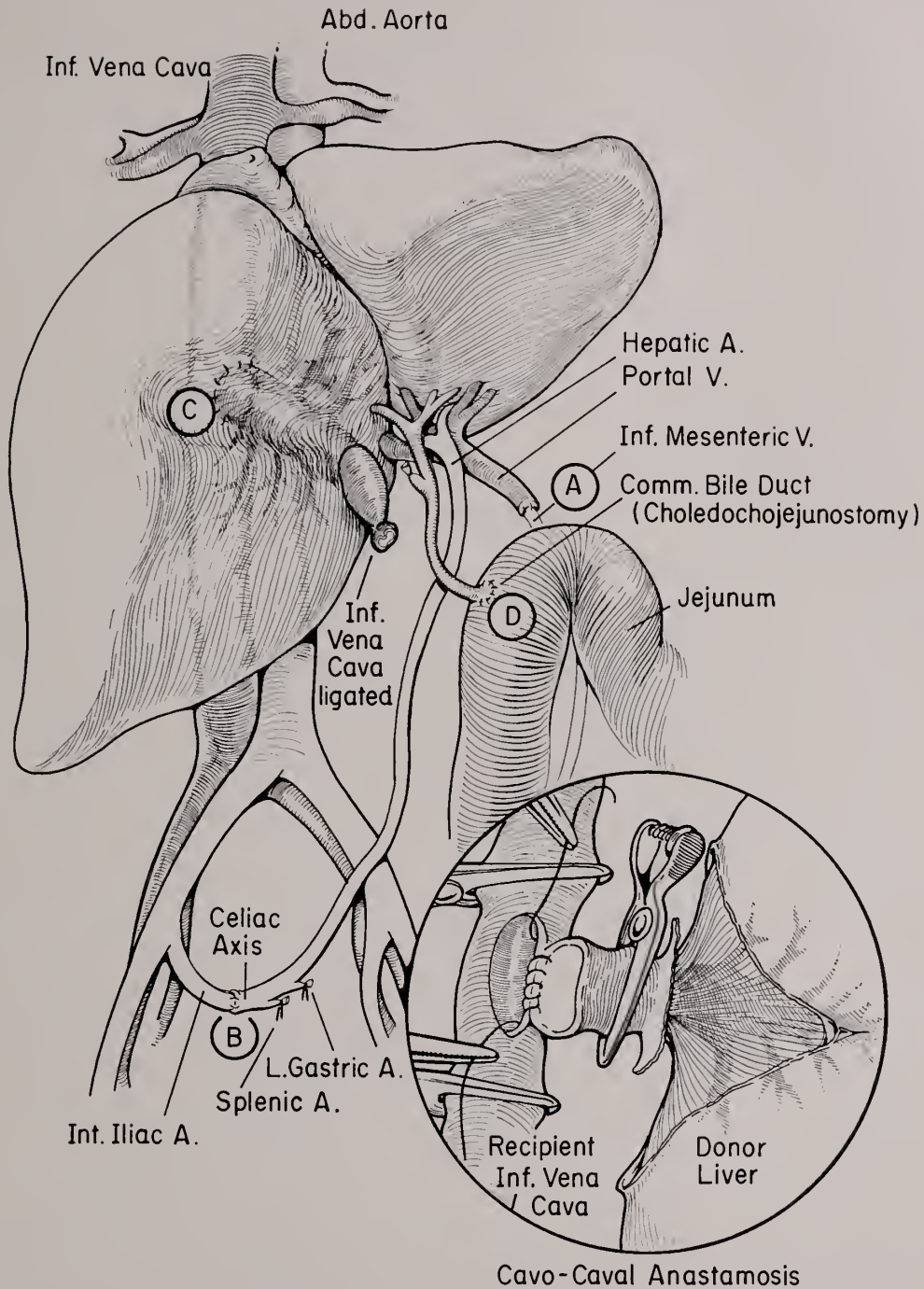


Fig. 1—Accessory Liver Transplant with Anastomoses completed: (A) Recipient Inferior Mesenteric Vein to Donor Portal Vein, (B) Recipient Internal Iliac Artery to Donor Celiac Axis Artery (Hepatic Arterial Supply), (C) Suprahepatic Vena Cava of Donor to Recipient Inferior Vena Cava and (D) Donor Common Bile Duct to Recipient Jejunum.

Inset—Anastomosis between the suprahepatic vena cava of the donor and the inferior vena cava of the recipient below the renal vessels—Suturing of the posterior wall of the anastomosis.

Continued

and who was already, as you have heard, in extremely deep coma. We did not know at the time to what extent his brain had suffered from the cardiac arrest before his surgery, and we decided therefore to give him the benefit of the doubt and attempt a liver transplant which either might of itself be permanently successful in functioning as a homograft or might, if rejected, enable his own liver to have sufficient time for recovery. Another unknown factor was the question of to what extent he still had circulating viremia or antibodies to the virus. If he still had circulating viremia without antibody formation then possibly the graft itself might be destroyed. We therefore searched for a suitable donor organ. The liver which we obtained was from the O group, which is regarded by Starzl's work as a universal donor and was therefore suitable for this patient. The liver was obtained after death of the donor by first opening the abdomen, by cannulating the portal vein and perfusing it with Ringer-lactate solution at 4°C. Fortunately, the liver showed evidence of adequate perfusion and had not suffered intra-hepatic thrombosis.

The organ was dissected out, taking with it the hepatic artery, the common bile duct, the portal vein and the inferior vena cava above and below the liver. That portion of the vena cava above the liver was divided close to the heart, and a rim of the diaphragm was removed with it. Several small veins on the posterior surface of the liver associated with the adrenal gland were divided and subsequently ligated. The organ was then placed in a dish, covered with ice-cold Ringer-lactate solution and transported to Metropolitan Hospital. There the recipient was opened and the inferior vena cava and the internal iliac artery were prepared. The first anastomosis was between the internal iliac artery of the recipient and the hepatic artery of the donor. The second anastomosis was between the vena cava of the recipient below the renal arteries and the suprahepatic donor vena cava, an end-to-side anastomosis. The inferior vena cava of the donor liver below that liver was tied off and the portal vein anastomosed in this instance to the inferior mesenteric vein of the recipient in order that the portal vein would be perfused with splanchnic blood and thus avoid the problem of liver shrinkage which has been discussed by Dr. Smith in the introduction. The final anastomosis was between the common bile duct and the upper jejunum. This particular donor liver was from an elderly lady who had gallstones. We therefore deemed it unwise to use the gallbladder for a cholecystenterostomy, as this might result in subsequent infection. We therefore did a cholecystectomy on the donor organ after it had been hooked up in the recipient—a donor cholecystectomy.

Dr. Mersheimer:

Thank you very much Dr. Cree. I want you to know that this remarkable piece of surgery was done by Dr. Cree and the surgical team at the Met. They completed this in something like six hours, which I think is fantastic.

The Coagulation Problem

Dr. Robert Goldstein:*

The problems in hemostasis which may arise in a patient such as the one we are discussing who undergoes a liver transplant can perhaps best be considered in three phases.

*Professor of Medicine, New York Medical College.

Preoperative Period

In the preoperative period, a coagulation defect may be present secondary to hepatocellular disease. Certain coagulation factors are produced in the liver: the vitamin K dependent factors (prothrombin, Factor VII, Factor IX and Factor X), Factor V, fibrinogen and probably Factor XI. The plasma levels of these factors are depressed in hepatocellular disease to a variable extent and roughly in proportion to the severity of the liver disease. This patient exhibited a marked decrease in the plasma levels of prothrombin, Factors V, VII, IX and X, but only a slight depression of fibrinogen. Factor XI was not determined. Thrombocytopenia may also be encountered in liver disease, particularly in the presence of congestive splenomegaly. The platelet count was within the normal range in this patient. The exchange transfusions temporarily improved coagulation by increasing the plasma levels of the deficient clotting factors. The exact rise in these factors was difficult to determine since heparinized blood was used for the transfusions and heparin interferes in our assay systems. It should be pointed out that any improvement obtained is of short duration since the half-life of the clotting factors involved, except for fibrinogen, has been reported to range from two to twelve hours. The patient's platelet count remained normal following the exchange transfusions as would be expected since fresh blood rather than bank blood was used. Had bank blood been used, thrombocytopenia undoubtedly would have been induced, for the platelets in bank blood are not viable *in vivo* and platelet production would not have kept pace with platelet removal. Although the fibrinolytic activity of the patient's blood was normal as determined by whole blood clot lysis and euglobulin lysis times, the second or operative phase might well have been complicated by an activation of the fibrinolytic mechanism. Stress has been shown to increase blood fibrinolytic activity in normal individuals presumably by the release of activators of the fibrinolytic mechanism. This response to stress in a patient with hepatocellular disease has been shown to be greater and of longer duration.

The Operative Period

Operative procedures in such patients may induce a severe fibrinolytic syndrome. The role of the liver in the control of *in-vivo* fibrinolysis is not clear. In our patient, although there was significant shortening of the euglobulin lysis time during the early phase of surgery indicating increased fibrinolytic activity, there was no progression to an overt fibrinolytic state, and the euglobulin lysis times returned to normal. Another complication of the operative phase might be the release of some factor from the donor liver which has an adverse effect on hemostasis. Dr. Cree has shown in animals that implantation of a liver stored for several hours at 5°C. would induce a hemorrhagic diathesis which could be partially eliminated by perfusion of the liver prior to transplantation. We found no evidence to indicate that in this case the transplanted liver induced any further deterioration of hemostasis. However, neither was there evidence that the transplanted liver improved the coagulation deficiencies.

Postoperative Period

We had little opportunity in this patient to study the third or postoperative phase. As Dr. Smith mentioned, in humans who have survived liver trans-

Continued

plantation for more than a few days, death was caused by or associated with intravascular coagulation, which may prove to be a very important problem in liver transplantation when it is possible to control graft rejection. At present, the cause of the intravascular coagulation remains obscure. From experimental data it appears that the liver normally plays a very important role in the maintenance of the fluidity of the blood by removing activated coagulation factors formed during the course of coagulation, which are necessary intermediaries for coagulation to progress to the point of completion or fibrin deposition. Evidence indicates that this is a function of the reticuloendothelial system of the liver. It could be postulated that if this function of the liver's R.E. system is impaired, the balance *in vivo* between the tendency for the blood to clot versus the inhibitory mechanisms would be shifted towards coagulation, and intravascular coagulation would occur with the production of thromboembolic phenomena and/or defibrination. Although we did a number of coagulation studies during the short postoperative period this patient survived, it was difficult for us to interpret them because of treatment the patient was receiving which included exchange transfusion with heparinized blood and hemodialysis with the use of heparin and protamine. It was evident, however, that the donor liver did not increase the plasma levels of the clotting factors which had been depressed because of liver failure.

The Postoperative Course

Dr. Smith:

On October 28, at 10:00 a.m., the patient was returned from the recovery room unconscious, receiving respiratory aid by means of a Bird respirator.

The Blood Pressure

The blood pressure remained at 70-80 systolic, and a urine output of 5 ml./hr. was raised to 16 ml./hr. with Mannitol. Ammonia levels remained at the 300-400 $\mu\text{gm}\%$ range. His hypovolemia was corrected with whole blood, packed cells and albumin. However, urinary output and central venous pressure remained low. During the afternoon, the ammonia level fell from 585 $\mu\text{gm}\%$ to 295 $\mu\text{gm}\%$, a preoperative bilirubin of 16 mg./100 ml. dropped remarkably to 7 mg./100 ml., and a preoperative prothrombin time of 45 seconds was halved. The blood pressure was maintained quite well with a titrated Aramine drip (200 mg./ltr.).

Pneumothorax

At 7:00 p.m. it was discovered that the patient had a bilateral pneumothorax. Chest tubes were inserted and connected to suction bottles. X-rays then revealed almost complete re-expansion of both lungs. Soon thereafter, the blood ammonia levels began to increase, oligurea continued, and electrolytes and urea levels remained at normal level.

On the morning of Saturday, October 29, a bilateral pneumothorax was again evident and larger caliber chest tubes were then employed. The bilirubin rose from 7 to 8 mg./100 ml., but the morning blood ammonia level was 1000 $\mu\text{gm}\%$. An abdominal sump drain recovered fluid having a high amylase content.

Hemodialysis

Hemodialysis using the left radial artery and left antecubital cephalic vein

was carried out by Dr. Treser for eight hours, and exchange transfusions were performed by Dr. Rothenburg. Additional blood was administered. Ammonia levels dropped dramatically to the 100-200 $\mu\text{gm}\%$ level, although the patient's clinical status remained unchanged. Abdominocentesis recovered 800 cc. of dark blood, and dark blood was obtained from the stomach.

During the night of October 29 the blood ammonia level was 152 $\mu\text{gm}\%$. Cedilanid was added to the regimen to combat a rising venous pressure of 11 cm. sodium chloride. The central venous pressure continued to rise to a peak level of 21 cm. sodium chloride. The ammonia level continued to remain low. Cardiac arrest occurred at 6:30 a.m. on the morning of October 30, 46 hours after the transplant.

Autopsy Findings

Dr. Alfredo La Porta:*

At autopsy, the arterial and venous anastomoses and cholechojejunostomy showed no evidence of dehiscence or leakage.

Recipient's Liver

The recipient's liver weighed 750 Gm. It was firm and a dark reddish-brown. The cut surfaces were mottled, without any distinct pattern, dark brown and congested in appearance. Microscopically there was massive destruction of hepatic cells, but with preservation of the supporting architectural framework. The preserved sinusoids were congested and the bile ducts unaffected.

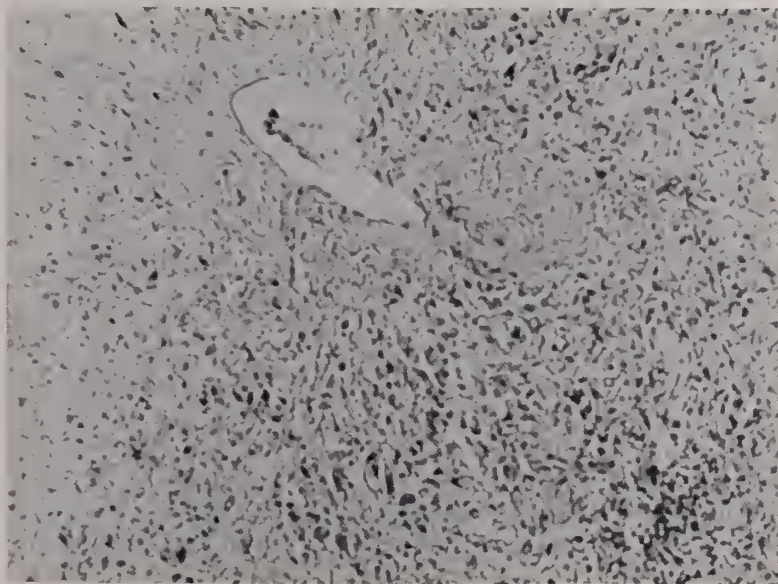


Fig. 2—Human liver transplant. Histological section of recipient liver removed at autopsy. Note the virtual absence of hepatocytes due to necrosis. (H. & E. $\times 440$)

The Donor's Liver

The donor's liver weighed 1180 Gm. It was soft and friable. Micro-

*Assistant Professor of Pathology, New York Medical College.

Continued

scopically there was widening of the sinusoids with minimal to moderate centrilobular congestion. The hepatocytes showed now and then minimal hydropic changes and granularity of the cytoplasm. Both lungs were diffusely consolidated by bronchopneumonic process of confluent type. Liquid and clotted blood had accumulated in the bronchial tree.

The kidneys were swollen with indistinct cortico-medullary junction. Microscopically the cortices showed diffuse ischemic necrosis and good preservation of the medullae. Hemorrhagic phenomena were observed in the heart, mucosa of the gastrointestinal tract, pancreas, and urinary bladder. A hemorrhagic suffusion was found in the mesentery and the retroperitoneal soft tissue, extending along dissecting planes into the mediastinal structures.

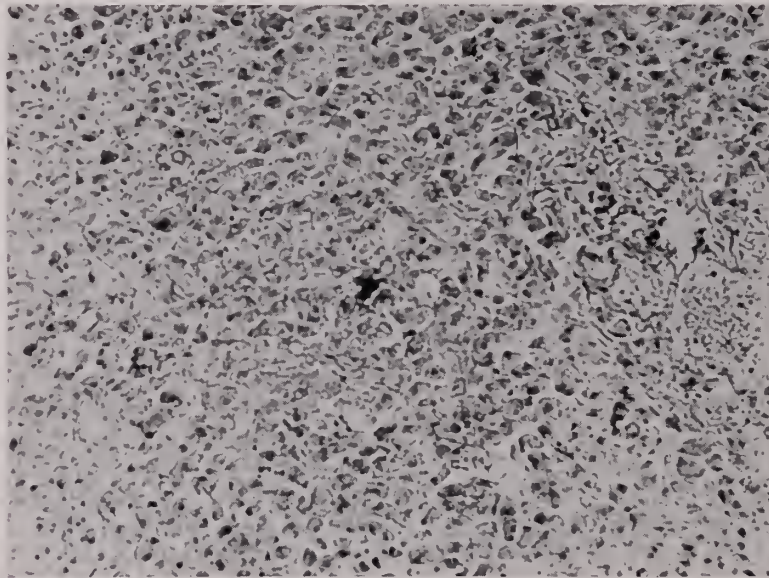


Fig. 3—Human liver transplant. Histological section of donor liver removed at autopsy. Note the minimal changes in the hepatocytes with good preservation of the hepatic architecture. (H. & E. $\times 440$)

Dr. Levine:

I am impressed with something which has come into evidence in the school and in the center here, and that is a full-scale type of cooperative effort involving many departments and many people working as a team. Now that Dr. Cree is here and there has been development in various areas in the Department of Medicine, with interest in coagulation, transfusions, hematological aspects, and renal aspects, I hope that the challenge of organ transplantation ushers in an era of extensive clinical effort involving the cooperative teams necessary for this kind of work.

Dr. Mersheimer:

Thank you very much, Dr. Levine.

Dr. Feit, our student who stayed up all night and took these pictures, has also been helping to project them; and I think that he deserves a good hand from all of us. I too would like to add to what Dr. Levine said because this could not have been possible without the complete cooperation of Dr. Rubin, Dr. Goldstein, Dr. Rosenthal and Dr. Treser and other supporting members

of the Department of Medicine. We certainly have appreciated everything that they have done, and we hope that this will continue to be a cooperative effort. If there are any questions from the audience, we can answer them; then we will ask Dr. Cree to close. Any question from the audience?

Question:

(Dr. Burman) I would like to know why in the case of these problems exchange transfusion does not work? Theoretically it should work.

Answer:

(Dr. Rosenthal) For one thing, working has several different connotations. Does working mean that the patient wakes up for 24 hours, or just improves his level of consciousness on a transient basis, or actually walks out of the hospital? Those are the possibilities. In the cases from South Africa, all patients responded; but two subsequently died. Our patient had a brief response to the first transfusion. One of the thoughts which occurred to us was that he might have suffered so much brain damage as a result of anoxia due to the cardiac arrest that he could not respond. Another factor to be considered is that during prolonged deep coma, cerebral metabolism may be so altered that permanent damage may occur. It is well known that brain oxygen and glucose uptake are markedly reduced during hepatic coma. A brain which is not utilizing oxygen or glucose may very well go on to irreversible damage.

Dr. Mersheimer:

We have thanked the Department of Medicine, but we can never forget that the Department of Anesthesia stayed with this patient throughout. Dr. Bizzarri, are there any comments you would like to make?

Irreversible Cerebral Damage

Dr. Dante Bizzarri:*

On October 27, 1966 (the day before surgery), the patient suffered a period of cardiac arrest which, though short in duration (30-60 seconds), caused irreversible cerebral damage as evidenced by persistent apnea. There is some doubt in my mind as to the precipitating cause of the arrest, but I suspect that it followed a prolonged period of suctioning thru the tracheotomy tube.

Decerebrate Rigidity

We began, then, with an apneic patient in deep coma and decerebrate rigidity. Although there was no need for anesthetics, twice during the operation a muscle relaxant had to be administered for abdominal relaxation. Because the patient had a temperature of 90°F. esophageal, he was placed on a thermo-blanket with the intent of warming him, but despite this, his temperature declined to 88°F. Throughout the operation the heart rate remained regular (70-90) and the electrocardiogram showed no abnormalities. The blood pressure (intraarterial) ranged between 100/80-70/60 mmHg. and at times had to be supported by small amounts of vasoconstrictors. The

*Assistant Clinical Professor of Anesthesiology, New York Medical College.

Continued

blood loss of 3000 cc. as calculated by continuous perdometer measurements was replaced by continuous transfusion. The central venous pressure ranged between 6-10 cm. of water.

By 5:00 a.m., the urinary output was 250 cc., but only 15 cc. were secreted from then to the end of the operation.

The main problem was the maintenance of adequate ventilation and oxygenation in the presence of a markedly reduced lung compliance. We were forced to use high positive pressure.

Four arterial blood samples were analyzed for pH, pCO₂, and pO₂.

Blood Gas Studies:

Time	3:31 a.m.	5:00 a.m.	6:00 a.m.	9:00 a.m.
pH	7.42	7.42	7.51	7.48
pO ₂	170mmHg.	200mmHg.	160mmHg.	210mmHg.
pCO ₂	40mmHg.	47mmHg.	42mmHg.	50mmHg.

The relatively low pO₂, despite the administration of 100% oxygen delivered at higher than normal tidal and minute volumes, was a clear indication of severe pulmonary disease.

Dr. Mersheimer:

Thank you, Dr. Bizzarri. Others that I want to thank are Miss Thieler and her group of O.R. nurses who got up in the middle of the night and stayed with Dr. Cree until the end. Dr. Cree, would you care to make any concluding remarks?

Dr. Cree:

I would like to thank Dr. Bizzarri particularly for all his work. His work and success in getting this patient off the table was absolutely indispensable. The administration of the curare, I think, was a particularly courageous step fraught with danger, but it was absolutely vital in carrying out this transplant and in getting the abdomen closed. The entire work of the Anesthesia Department in helping us during the postoperative period was an indispensable part of the care of this patient. I would also like to thank all the residents, both medical and surgical, whose efforts were superhuman in looking after this patient continuously over a period of well over 48 hours. The co-operative efforts of everyone were magnificent and played no small part in getting this patient as far as he did get. That we were not successful in prolonging his survival at least for a period of weeks, I think in the last analysis was almost certainly associated with the cerebral damage which he had already received. Whether this was due to anoxia or whether the high levels of ammonia which he sustained would produce irreversible brain damage, we do not know, and I think that only future trials of this type of work in cases of transplantation will provide the answers. We learned a tremendous amount as regards the techniques and coagulation problems involved, for which we are very grateful to Dr. Goldstein and Dr. Galanakis. We also learned a great deal about the administrative problems and those of ward care and the sort of rooms and equipment required. I think that we will almost certainly be able to overcome the early problems of liver trans-

plantation in these patients. The late problems, as far as we know at this time, are identical with those in kidney transplants, namely, problems of infection, especially bizarre infections by monilia, pneumocystis carinii and so forth, and the problem of rejection when insufficient immunosuppressive drugs are administered. It is this delicate path of steering between rejection and infection which is the challenge of the postoperative care of all patients with organ transplants.

Walter L. Mersheimer, M.D.
New York, New York

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References

1. Goodrich, E. O., Jr.; Welch, H. F.; Nelson, J. A.; Beecher, T. S.; and Welch, C. S.: Homotransplantation of the Canine Liver. *Surgery*, 39:244, 1956.
2. Sicular, A.; and Moore, F. D.: The Postmortem Survival of Tissues II: The Effect of Time and Temperature on the Survival of Liver as Measured by Glucose Oxidation Rate. *J Surg Res* 1:16, 1961.
3. Moore, F. D.; Smith, L. L.; Burnap, T. K.; Dallenbach, F. D.; Dammin, G. J.; Gruber, V. F.; Shoemaker, W. C.; Steenburg, R. W.; Ball, M. R.; and Belko, J. S.: One Stage Homotransplantation of the Liver Following Total Hepatectomy in Dogs. *Transplantation* 6:103, 1959.
4. Starzl, T. E.; Kaupp, H. A., Jr.; Brock, D. R.; Lazarus, R. E.; and Johnson, R. V.: Reconstructive Problems in Canine Liver Homotransplantation with Special Reference to the Postoperative Role of Hepatic Venous Flow. *Surg Gynec Obstet* 111:733, 1960.
5. Starzl, T. E.; Marchioro, T. L.; Rowlands, D. T. Jr.; Kirkpatrick, C. H.; Wilson, W. E. C.; Rifkind, D.; and Waddell, W. R.: Immunosuppression After Experimental and Clinical Homotransplantation of the Liver. *Ann Surg* 160:411, 1964.
6. Starzl, T. E.; Marchioro, T. L.; Porter, K. A.; Taylor, P. D.; Faris, T. D.; Herman, T. J.; Hlad, C. J.; and Waddell, W. R.: Factors Determining Short- and Long-Term Survival After Orthotopic Liver Homotransplantation in the Dog. *Surgery* 58:131, 1965.
7. Starzl, T. E.; Marchioro, T. L.; Porter, K. A.; and Faris, T. D.: The Role of Organ Transplantation in Pediatrics. *Pediat Clin N Amer* 13:386, 1966.
8. von Kaulla, K. N.; Kay, H.; von Kaulla, G.; Marchioro, T. L.; and Starzl, T. E.: Changes in Blood Coagulation. *Arch Surg* 92:71, 1966.
9. Marchioro, T. L.; Porter, K. A.; Brown, B. I.; Faris, T. D.; Herman, T. J.; Sudweeks, A. and Starzl, T. E.: The Specific Influence of Non-Hepatic Splanchnic Venous Blood Flow on the Liver. *Surg Forum* 16:280, 1965.
10. Halgrimson, C. G.; Marchioro, T. L.; Faris, T. D.; Porter, K. A.; Peters, G. N.; and Starzl, T. E.: Auxiliary Liver Transplantation: Effect of Host Portocaval Shunt. *Arch Surg* 93:107, 1966.
11. Katz, R.; Velasco, M.; Klinger, J. and Alessandri, H.: Corticosteroids in the Treatment of Acute Hepatitis in Coma. *Gastroenterology* 42:258, 1962.
12. Berger, R. L.; Liversage, R. M., Jr.; Chalmers, T. C.; Graham, J. H.; McGoldrick, D. M.; and Stohlman, F., Jr.: Exchange Transfusion in the Treatment of Fulminating Hepatitis. *New Engl J Med* 274:497, 1966.
13. Trey, C.; Burns, D. G.; and Saunders, S. J.: Treatment of Hepatic Coma by Exchange Blood Transfusion. *New Engl J Med* 274:473, 1966.

There is all the difference in the world between a man who knocks you down and a man who leaves you alone.

**Resolution Adopted by the Board of Directors
of the American Cancer Society, May 5, 1967**

Whereas, scientific evidence has established cigarette smoking as the major known cause of cancer deaths; and

Whereas, it has been estimated by the Surgeon General of the United States that as many as 300,000 excess deaths may be attributable to the effects of cigarette smoking; and

Whereas, cigarette smoking has been causally related to several million extra cases of serious illness and disability annually in the United States; and

Whereas, medical and public health institutions and personnel have a special responsibility to discourage practices that are harmful to health; and

Whereas, physicians have notably reduced their cigarette smoking (ten years ago 60% smoked cigarettes; today, less than 30%):

Now, Therefore, Be It Resolved that the American Cancer Society urge:

1. That physicians, dentists, nurses and other medical personnel do everything possible to reduce further cigarette smoking both by example and by advice concerning the health hazards of smoking, and
2. That the sale of cigarettes by medical and health institutions be discontinued, and
3. That hospitals, clinics, health centers and physicians' and dentists' offices discourage smoking by personnel and patients through appropriate restrictions and signs.

Come What Might, I Would Be a Doctor of Medicine

It may seem strange that I remember him, for he died in '83 when I was not quite ten years old. But, although not talkative, (my father) had a powerful and attractive personality. This brought him tremendous popularity and a large clientele. He was what doctors were in those days—both physician and surgeon, but it was his great skill in surgery that filled his offices.

When Garfield was shot, he was called in—quite too late. It has always been my belief that had he and Agnew been given a free hand, the pitiful death of one martyred President might have been avoided. However, this is merely the faith of a devoted son that speaks.

Those offices of his had an irresistible fascination for me. Father said I was too serious for a child, because I sought my companions among older people. I must have been an odd little figure, flitting in and out of those crowded waiting-rooms and talking with any whom I could engage in conversation. . . . In fact, he used to take me with him in his sleigh in winter to the Children's Hospital; and he even took me to see his patients when he made his rounds to their homes.

His death at only forty-one years of age was a fearful shock. At my grandmother's, where I had been taken in order to leave our home as quiet as possible, they woke me up in the night—I had been dreaming that he was dying—and told me. It had never entered my head that so strong, wise, and beloved a man could die.

His death did two things to me: first, I definitely decided that prayers were not answered and that Dr. Sunderland, our pastor, was wrong in supposing that God was merciful; and second, I resolved that, come what might, I would be a Doctor of Medicine.*

*Bailey Ashford (1873-) in *Why We Became Doctors*, edited by Noah Fabricant, 1954.

A large, dark, grainy microscopic image showing numerous spermatozoa with long, wavy tails. In the upper left corner, there is a smaller, square inset showing a different view of spermatozoa, which appear more clustered and less motile.

New view of an oral contraceptive at work

Although suppression of ovulation remains the primary mode of action of oral contraceptives, newer knowledge indicates that products like Norinyl-1— a combination of both low-dosage progestogen and estrogen for the full treatment cycle— may provide multiple action that helps explain their unexcelled record of contraceptive effectiveness. This report explores the possible secondary protective mechanisms offered by combined hormonal administration.

Accumulating evidence has indicated that sparse, highly viscous cervical mucus has a possible adverse effect on the motility and survival of spermatozoa.

The estrogen-opposing progestational ingredient of Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.) changes the usual mid-cycle picture of a thin, watery cervical mucus. The result—a built-in barrier that appears to inhibit sperm from reaching the ovum should one be released. The inset in the adjoining photograph shows immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

How the estrogen-opposing action of Norinyl-1 creates cervical mucus that may be hostile to sperm penetration

Normally, estrogen activity during the fertile midcycle stimulates the production of a profuse and watery cervical mucus that permits maximum sperm motility and promotes penetration.

But what happens when Norinyl-1 is administered? Its potent progestogen, norethindrone, opposes estrogen stimulation of cervical mucus. Consequently, the amount of mucus decreases and its viscosity increases. This results in a sparse but thick mucus barrier that appears to diminish the vitality of the sperm and to impair its powers of penetration.

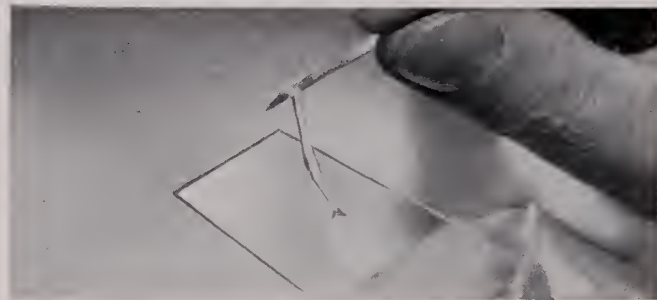
The role of viscous cervical mucus as a secondary action of Norinyl-1

In a report on 89 patients taking this medication,* cervical mucus obtained from cycle day 5 to cycle day 29 appeared scant and thick and exhibited little or no Spinnbarkeit.

In the opinion of this investigator, the effect on cervical mucus may be sufficient to prevent conception.

*Cohen, M. R.: Symposium: Mechanisms of Action of Low Dosage Oral Contraceptive, Yale University Medical Center, New Haven, Conn., April 6, 1967.

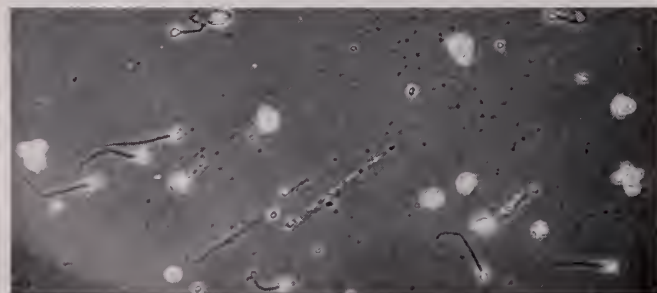
Normal cervical mucus at midcycle in untreated patient is known to permit sperm motility... promote sperm penetration.



Cervical mucus is thin and watery with a stretchability (Spinnbarkeit) of 15 to 20 cm.



Thin, watery mucus crystallizes into this well-defined, fernlike pattern within a minute.

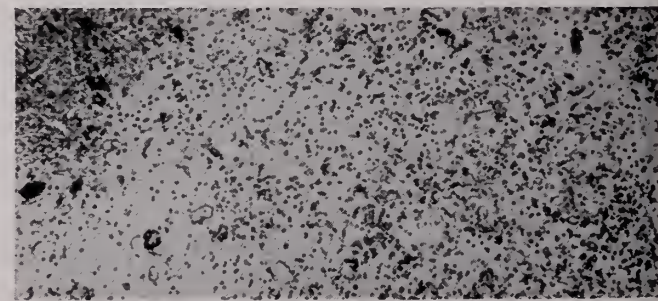


Spermatozoa appear healthy, are active and freemoving.

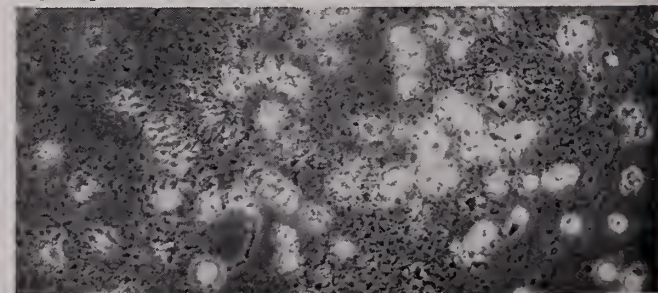
Viscous cervical mucus at midcycle produced by Norinyl-1 appears to impair sperm vitality... inhibit penetration.



Cervical mucus is scanty, thick and viscous. Spinnbarkeit is 1 cm. or less.



In thick, viscous cervical mucus the fern pattern is poorly defined or absent.

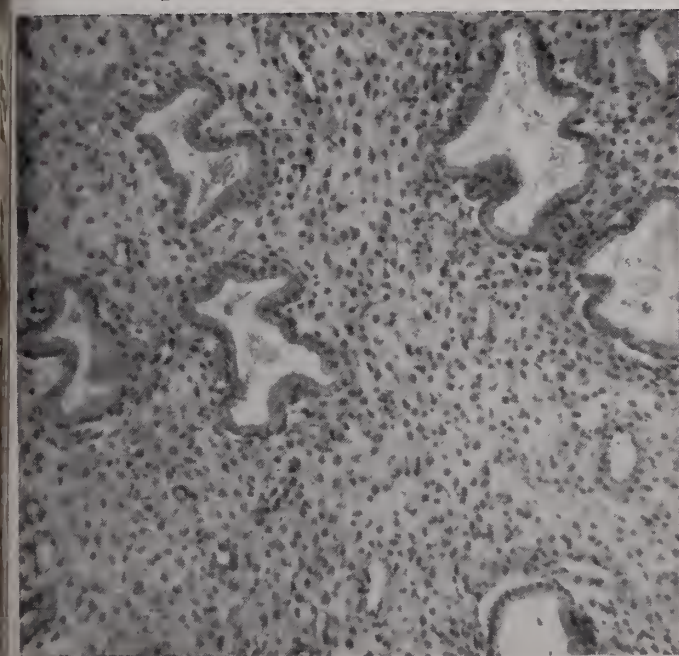


Immobile spermatozoa as they appear in cervical mucus taken from a patient treated with Norinyl-1.

How Norinyl-1 alters normal endometrial responses— another possible protective mechanism

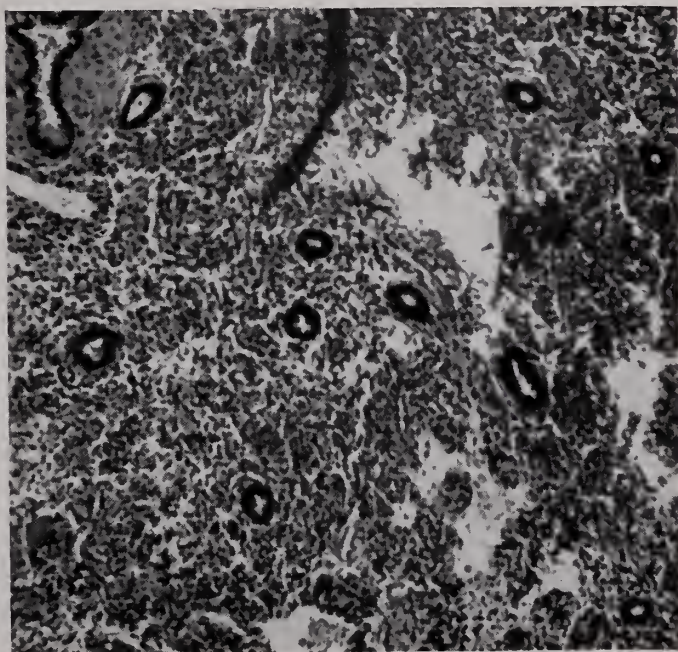
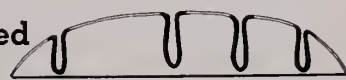
Let us suppose that an ovum is released—as occurs in an occasional, rare case—and somehow a sperm succeeds in penetrating the cervical mucus barrier. Should this come about, the additional action of Norinyl-1 may protect the patient from unwanted pregnancy. The theory is that progestogen intake makes endometrial tissue unreceptive to implantation.

Endometrium of
untreated patient



Normally, the endometrium progresses through a proliferative phase stimulated by estrogen and a secretory phase stimulated by progesterone. During the secretory phase the endometrium is receptive to the fertilized ovum.

Endometrium produced
by Norinyl-1



When Norinyl-1 is administered its progestogen component—norethindrone—accelerates the secretory phase and suppresses glandular and vascular development.

new
Norinyl-1[®]
(norethindrone 1mg. $\bar{c}$ mestranol 0.05mg.) **tablets**

See last page for contraindications, precautions, side effects and dosage.

effective fertility control
on half the previous dosage

maintains ratio
of the established
norethindrone/mestranol
combination

lower cost

new Norinyl-1[®]

(norethindrone 1mg. $\bar{c}$ mestranol 0.05mg.) tablets

Reduction of oral contraceptive dosage to lowest effective levels has become a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now available in a new strength in which both norethindrone and mestranol are reduced 50 percent. Studies show that Norinyl-1 achieves fertility control with only 1.05 mg. of combined progestogen and estrogen per tablet.

Norethindrone was first reported for use as a progestational agent in human beings in 1955. Norethindrone 2 mg. with mestranol 0.1 mg., as an oral contraceptive, is currently in use by over 2,000,000 women. Clinical experience now establishes that Norinyl-1 also amply meets the criteria of reliability and safety.*

*Symposium on Low-Dosage Oral Contraception, Palo Alto, Calif., July 15, 1965.

PRESCRIBING INFORMATION

Contraindications: 1. Patients with thrombophlebitis or with a history of thrombophlebitis or pulmonary embolism. 2. Liver dysfunction or disease. 3. Patients with known or suspected carcinoma of the breast or genital organs. 4. Undiagnosed vaginal bleeding.

Warnings: 1. Discontinue medication pending examination if there is sudden partial or complete loss of vision or if there is a sudden onset of proptosis, diplopia, or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. 2. Since the safety of Norinyl-1 in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods, pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule, the possibility of pregnancy should be considered at the time of the first missed period. 3. Detectable amounts of the active ingredients in oral contraceptives have been identified in the milk of mothers receiving these drugs. The significance of this dose to the infant has not been determined.

Precautions: 1. The pretreatment physical examination should include special reference to breast and pelvic organs, as well as a Papanicolaou smear. 2. Endocrine and possibly liver function tests may be affected by treatment with Norinyl-1. Therefore, if such tests are abnormal in a patient taking Norinyl-1, it is recommended that they be repeated after the drug has been withdrawn for 2 months. 3. Under the influence of estrogen-progestogen preparations, preexisting uterine fibroids may increase in size. 4. Because these agents may cause some degree of fluid retention, conditions that may be influenced by this factor, such as epilepsy, migraine, asthma, cardiac, or renal dysfunction, require careful observation. 5. Although a cause and effect relationship has not been established, Norinyl-1 should be used with caution in patients with a history of cerebrovascular accident. 6. In relation to breakthrough bleeding, as in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are

indicated. 7. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. 8. Any possible influence of prolonged Norinyl-1 therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. 9. A decrease in glucose tolerance has been observed in a small percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Norinyl-1 therapy. 10. Because of the occasional occurrence of thrombophlebitis and pulmonary embolism in patients taking oral contraceptives, the physician should be alert to the earliest manifestations of the disease. A cause and effect relationship has not been demonstrated. 11. Because of the effects of estrogens on epiphyseal closure, Norinyl-1 should be used judiciously in young patients in whom bone growth is not complete. 12. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask the onset of the climacteric. 13. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

Side Effects: The following adverse reactions have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma, breast changes (tenderness, enlargement and secretion), loss of scalp hair, change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, erythema multiforme, erythema nodosum, hemorrhagic eruption, migraine, rash (allergic), itching, rise in blood pressure in susceptible individuals, mental depression.

The following occurrences have been observed in users of oral contraceptives. A cause and effect relationship has not been established: thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory results may be

altered by the use of oral contraceptives: increased bromsulphalein retention and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in T₃ values), metapyrone test, pregnane diol determination.

Other side effects reported to have occurred in association with use of this drug are dizziness, hirsutism, pains in legs, back, chest and abdomen, dysuria, drowsiness, vaginal discharge, libido increased and decreased, eruptions, hypermenorrhea, hypomenorrhea, increased appetite, G.U. infections, varicose veins, abdominal fullness, acne, headache, nervousness, allergies, blurred vision, pain in eyes, and itching in eyes. For complete clinical data, see package insert.

Dosage and Administration: 1. One tablet of Norinyl-1 is administered orally for 20 days beginning on day 5 of the menstrual cycle. (Count day 1 of the cycle as the first day of menstrual bleeding.) Repeat this dosage schedule for each cycle. 2. If no menstrual period occurs after a cycle of treatment (20 tablets) in which patient adhered to the schedule, the patient must be instructed to resume taking the Norinyl-1 tablets 7 days after the previous 20-day course was completed. For example, if the last pill of a previous cycle had been taken on a Sunday, then a new cycle of treatment should begin on the following Sunday. 3. In the postpartum woman, it is recommended that the first cycle of treatment should begin on day 5 of the first menstrual cycle. However, Norinyl-1 should not be administered during lactation.

Availability: Norinyl-1 (norethindrone 1 mg. with mestranol 0.05 mg.)—Dispensers of 20 and 60 and bottles of 250 tablets.

norethindrone — an original steroid from
SYNTEX
LABORATORIES INC., PALO ALTO, CALIF.

Medical Seminar

Syncope

Simple or Serious?

Presented as a Seminar

Sponsored by

The Faculty of the Mayo Graduate School of Medicine

SYNCOPE is that loss of consciousness due to an acute decrease of cerebral blood flow.¹ Although quite common in human experience, only when it is recurrent does the patient consult a physician. While most fainting experiences are trivial, sometimes they are indicative of a serious disorder, and rarely is the faint irreversible with sudden death ensuing. All too often the physician merely attempts to exclude a convulsive disorder and, having done so, relegates the patient's symptoms to the category of "the simple faint."²

Syncope is a symptom of a large number of disorders, having certain precipitating factors, warning signs, characteristic features during the unconscious period, and certain post-syncopal residua. The history is inadequate if the physician inquires only into the syncopal attack itself: whether or not there were convulsions, urinary or fecal incontinence, biting of the tongue, sweating, or pallor. Often overlooked are such factors as lack of food, degree of fatigue, emotional factors, position and activity of the body at the onset of syncope, environmental temperature, and any recent illnesses requiring prolonged bedrest. One must not overlook any warning symptoms such as angina, cardiac irregularities, paresthesias, vertigo, or any involuntary movements. There may have been no warning symptoms.

Usually syncope is classified according to the underlying physiological mechanism; but this

tends to be cumbersome, especially when more than one mechanism is operating.

Vasovagal Syncope

This is the classic simple faint. The warning symptoms may be abolished by atropine; yet the patient still faints.³ He is almost always in the upright position at the onset of the attack.

This form of syncope is a general response of the organism to fear or injury. Many of the physiological changes present are commonly seen with fear, but flight is not possible. Active vasodilatation in muscles occurs in preparation for flight, but there is no compensatory increase in muscular activity to aid venous return; nor does the cardiac output increase. Marked fall in blood pressure occurs as a result of the vasodilatation with sudden acute loss of arteriolar tone.⁴

Barcroft et al.⁵ have shown that at the time the blood pressure falls, there has been marked decrease in peripheral resistance, much of which can be accounted for by increased blood flow to muscle, amounting to the shunting of as much as 1500 ml. of blood per minute. Uvnas⁶ found that the vasodilatation in muscle is mediated through cholinergic sympathetic vasodilator fibers. Using the human centrifuge, Cohen and Silverman⁷ demonstrated that blackout occurs at a much lower "G" when the subject is afraid than when he is either confident

Continued

or defiant. In the former situation, he secretes predominantly epinephrine, while in the latter norepinephrine is secreted.

Orthostatic Hypotension

This differs from vasovagal syncope chiefly in that the circulatory disturbance is more chronic, so that fainting tends to occur repeatedly upon assuming the erect position.

Adaptive Mechanism

Certain adaptive mechanisms are required in man to counteract the gravitational effect upon circulating blood. Without these mechanisms, excess pooling of blood occurs in the lower extremities on standing, and the cerebral blood flow is markedly reduced. These mechanisms include:⁸

1. Peripheral vasoconstriction, which is mediated through pressor receptors in the aortic arch and carotid sinus via the vasomotor centers and sympathetic outflow.
2. Reflex tachycardia, which occurs concurrently with arteriolar constriction and aids in maintaining cardiac output.
3. Reflex augmentation of respiration and increased muscle tone, both mechanisms increasing venous return.
4. Reflex venous constriction which resists pooling of blood and forces blood from the venous reservoir into the circulation.

Reaction to Assumption of Upright Position

The normal reaction when tilted from recumbency to the erect position is an immediate drop in systolic pressure of 5 to 40 mm. Hg., but with a prompt rise, so that within 30 seconds the pressure equals or exceeds that at the recumbent level. But, as with many physiologic control systems, there is a wide variation in effectiveness even among normal persons, and some healthy individuals have poor postural adjustment. They complain of dizziness or faintness on standing, but the symptoms are generally mild or transient and usually seen in tall thin individuals with poor muscle tone or in those who have recently been subjected to prolonged bed rest.

Barker,⁹ in 1933, stated that for the diag-

nosis of orthostatic hypotension there must be an immediate, persistent, and consistent drop of at least 50 mm. Hg. systolic and a corresponding but smaller drop in diastolic pressure. Reflex tachycardia on standing is often but not always absent. Likewise, there are no symptoms of autonomic overactivity prior to the loss of consciousness.

Differential Diseases

Orthostatic hypotension was first described by Bradbury and Eggleston¹⁰ who noted its occurrence in diseases of the nervous system and emphasized the classical triad of postural hypotension with syncope, anhidrosis,* and impotence. This syndrome may be seen as part of the clinical picture in many diseases of the nervous system, both central and peripheral, and in several endocrinologic and metabolic disorders. The following is only a partial list of such diseases: craniopharyngioma, parasellar and posterior fossa tumors, multiple brain infarcts, Wernicke's encephalopathy, tabes dorsalis, syringomyelia,* porphyria, hypopituitarism, hypothyroidism, Addison's disease, and the peripheral neuropathy due to diabetes or amyloidosis. Sympathectomy or ganglionic blocking agents may be responsible. Micturition syncope seems to be merely a special type of orthostatic hypotension.

After the above disorders have been excluded, there still remain some patients in whom an underlying disease cannot be found. As one might expect, they are labeled as having idiopathic orthostatic hypotension,¹¹ which appears to be a primary degenerative disease of the nervous system beginning in the autonomic tracts. Eventually there may be progressive bilateral symmetrical involvement of the motor systems—corticospinal and corticobulbar tracts, basal ganglia, and cerebellum. This is manifested clinically by a variable picture in which Parkinsonian features, hyperreflexia, and pathologic reflexes may be seen, together with such signs of autonomic involvement as anisocoria and varying degrees of anhidrosis.

The basic disturbance in orthostatic hypotension is an autonomic dysfunction which results in impaired arteriolar constriction on standing. As can be seen from the above, the defect may occur at any level of the reflex arc

*See Test Your Word Score Page 1513.

—hypothalamus, brain stem, spinal cord, or peripheral nerve.

Luft and von Euler¹² showed decreased spontaneous excretion of norepinephrine in this condition. Hickler¹³ confirmed this and found a diminished norepinephrine response to tilt-table testing. Aldosterone excretion is reduced, probably due to lack of a stimulus for its secretion.

Cardiac Dysfunction

Cardiac arrhythmias, ischemic heart disease, congenital cardiac anomalies, and valvular disease may all give rise to syncope. The lesion may be extracardiac, influencing the heart on a reflex basis. It should be remembered that not all fainters who happen to have heart disease have their syncope on a cardiac basis. The onset of cardiac syncope is often quite abrupt, frequently without warning symptoms, and occurs independently of the position of the patient. Many patients with cardiac syncope have some convulsive movements while unconscious.

Stokes-Adams Syndrome

Stokes-Adams syndrome is the classic condition in which a cardiac arrhythmia results in syncope. The syncope is not due to the slow heart rate per se, but rather to asystole or ventricular fibrillation which occurs during the transition from partial to complete heart block. Rowe and White¹⁴ mention patients with heart block who were able to tolerate pulse rates in the twenties while ambulatory, and from five to 10 while recumbent, without experiencing syncope.

Myocardial Infarction

Loss of consciousness rarely occurs following angina pectoris in the absence of valvular disease but is fairly frequent in myocardial infarction, and here it is apt to be severe and prolonged. The loss of consciousness may be due to any one or a combination of the following factors: intense pain, arrhythmias, reflexes arising from coronary vessels, or a diminished stroke volume from a weakened myocardium. Persistence of the signs of vasomotor collapse, including pallor and sweating, in the post-syncopal period should alert the physician to the possibility of myocardial infarction, espe-

cially in the patient over 40.

Aortic Stenosis

Cowper,¹⁵ in 1706, first noted the common occurrence of syncope in patients with aortic stenosis. Hammersten¹⁶ studied 63 patients with this disease and found recurrent syncope to be present in 12. Seventy-five per cent of the patients with syncope had angina pectoris, and 94% of this group showed radiographic evidence of left ventricular enlargement. This is the classic example of "effort syncope," for in the great majority the faint occurs during or soon after exertion, and in most it is preceded by angina pectoris. Sometimes the faint can be aborted by standing still. The exact mechanism responsible for the loss of consciousness is not known. Electrocardiograms taken during the syncopal period have failed to reveal any consistent pattern. The fact that effort usually precipitates the faint and that it is often accompanied by angina suggests that there is inadequate outflow through the stenosed aortic valve, leading to both coronary and cerebral insufficiency. Peripheral resistance falls during exercise, but normally this is compensated for by augmented cardiac output, which fails to occur in aortic stenosis.

A few patients with syphilitic aortic insufficiency faint during exertion, presumably due to involvement of the coronary ostia.

Congenital Heart Disease

Patients with the cyanotic forms of congenital heart disease may faint after exertion. This is most commonly seen in children with tetralogy of Fallot.* Exercise increases the removal of oxygen in skeletal muscle, and markedly unsaturated venous blood enters the right side of the heart, a portion of this oxygen-poor blood passing through the shunt to the left ventricle and out to the body. As the blood flow through the lungs is little increased, the arterial oxygen saturation drops rapidly, and the patient loses consciousness as a result of cerebral anoxia.¹⁷

Irritable Carotid Sinus

A hyperirritable carotid sinus may lead to cardiac syncope on a reflex basis. Although the occurrence of significant cardiac slowing

Continued

*See Test Your Word Score Page 1513.

and even asystole on carotid sinus massage is fairly common, spontaneous fainting from this cause is not. In making this diagnosis one should satisfy himself that the induced faint is identical with the spontaneous faint; asystole is long enough to produce symptoms; and fainting has not been produced by massage or occlusion of the artery below the sinus. Usually there is vagal bradycardia with subsequent fall in blood pressure—the so-called “cardio-inhibitory type.” Other types have been described but are either rare or unproven. A hypersensitive carotid sinus may occur with arteriosclerosis or thrombosis of the carotid artery, neoplasms or inflammations in the neck, carotid body tumors, and digitalis toxicity. Cardiac syncope in the presence of atrial fibrillation may be due to a digitalis-potentiated stimulation of a hypersensitive carotid sinus.¹⁸

Pulmonary Disorders

Tussive syncope is the fainting which accompanies a severe bout of coughing, usually seen in middle-aged athletic men who have a history of chronic bronchitis. There appear to be two mechanisms underlying the syncope. A greatly increased intrathoracic pressure, which may reach 250-300 mm. Hg., develops during the episode, is transmitted to the cerebrospinal fluid compartment, and squeezes blood from the cranium so that the brain rapidly becomes anoxic. The increased intrathoracic pressure also results in decreased venous return to the heart with fall in cardiac output.¹⁹

Effort syncope may be found in pulmonary hypertension, either primary or secondary, its basis being a decreased cardiac output. As the right ventricle fails, there is a gradual fall in systemic pressure.

Syncope Due to CNS Disorders

Syncope is uncommon in diseases of the cerebrovascular system. When it does occur there is usually advanced occlusive disease of several of the large neck vessels. Focal neurological signs generally accompany the cerebral ischemia, and syncope is often without warning and prolonged. Syncope due to occlusive disease of the carotid artery usually does not occur un-

less the disease is bilateral or a hypersensitive carotid sinus is present.²⁰ Digital compression of the carotid artery, in order to induce syncope, should be avoided when occlusive vascular disease is suspected.

Syncope has been thought to be due in some cases to localized cerebral vasospasm. Weiss and Baker²¹ described a type of syncope in which carotid sinus stimulation causes unconsciousness within three to four seconds without alteration of blood pressure or heart rate. They felt it was due to a reflex acting on the mid-brain center regulating consciousness. Localized cerebral vasospasm has been incriminated as responsible for the syncopal attacks rarely seen in migraine, hypertensive encephalopathy, neurocirculatory collapse, and cough syncope.

Diagnosis

Neurologic Examination

Having obtained a careful history from the patient and any witnesses, and after excluding such conditions as may be confused with syncope—such as epilepsy, vertigo, hyperventilation, hysteria, and migraine—a detailed general and neurological examination must be performed in an attempt to uncover the underlying condition responsible for the recurrent syncopal attacks. Specific findings, such as postural hypotension, heart block, or advanced peripheral neuropathy, will be important clues to the nature of the spells. In the majority of patients, however, examination will show either no abnormalities or nonspecific findings that must be interpreted with prudence. A causal relationship between signs and symptoms must be established.

Laboratory Tests

Electroencephalography is generally of help only in separating epilepsy from syncope, not in the diagnosis of syncope, as here the interictal record is usually normal.²² In a study of syncope among 195 college students, Williams and Allen²³ found no correlation between incidence of electroencephalogram abnormalities and incidence of loss of consciousness. Gastaut and Fischer-Williams²⁴ found normal records in 83% of 218 patients with syncope. Ades,²⁵

however, found a much higher incidence of electroencephalogram abnormalities in pilots who had lost consciousness during flight. Had his criteria been used in selection of pilot candidates, 75% of the individuals involved would have been eliminated from flight school.

Electrocardiograms are of value only if they are unequivocally diagnostic of a cardiac disorder which may be associated with loss of consciousness.

Provocative measures such as carotid sinus massage, tilt-table testing, and hyperventilation may be carried out. Positive results can be diagnostic only when they produce symptoms identical to those in the spontaneous attacks.

One should be cognizant of the relative frequency of the causes of syncope. In 1961 Wayne categorized 510 patients with this complaint (see Table).²⁶

Conclusion

Syncope is usually a benign transitory condition. Occasionally it may indicate the presence

*Resident in Medicine, Mayo Graduate School of Medicine (University of Minnesota).

Causes of Syncope in 510 Patients
(Wayne, 1961)²⁶

Precardiac		343
Vasovagal Syncope	298	
Orthostatic Hypotension		
Chronic	28	
Postmicturition	17	
Cardiopulmonary		71
Arrhythmias & Heart Block	25	
Carotid Sinus Syncope	15	
Tussive Syncope	13	
Valvular Heart Disease	9	
Ischemic Heart Disease	7	
Pulmonary Hypertension	2	
Congenital Heart Disease	0	
Postcardiac		54
Epilepsy	26	
Cerebrovascular Disease	24	
Migraine	2	
Hypertensive Encephalopathy	2	
Others		19
Blood (e.g., hypoglycemia, anemia)	0	
Psychogenic		
Hyperventilation	15	
Hysteria	4	

of a serious, potentially fatal, organic disorder. It is for this reason that repetitive syncopal attacks should alert the physician and lead to a careful and systematic search for underlying disease.

E. Peter Pequegnat, M.D.*
Rochester, Minnesota

References

1. Sharpey-Schafer, E. P.: Emergencies in General Practice: Syncope. Brit Med J 2:506, 1956.
2. Engel, G. L.: Fainting: Physiological and Psychological Considerations. Ed. 2. Springfield. Charles C Thomas, Publisher, 1962, 196 pp.
3. Ibid.
4. Thomas, J. E. and Rooke, E. Douglas: Fainting. Proc Mayo Clin 38:397, 1963.
5. Barcroft, H. et al: Posthemorrhagic Fainting: Study by Cardiac Output and Forearm Flow. Lancet 1:489, 1944.
6. Uvnas, B.: Sympathetic Vasodilator System and Blood Flow. Physiol Rev (Suppl 4):69, 1960.
7. Cohen, S. J. and Silverman, A. J.: Psychophysiological Variations of Vascular Response Variability. J Psychosom Res 3:185, 1959.
8. Thomas, J. E., Molnar, G. D. and Schirger, A.: Orthostatic Hypotension: A Clinical Review. J Indian Med Prof 10:4698, 1963.
9. Barker, N. W.: Postural Hypotension: Report of a Case and Review of the Literature. Med Clin N Amer 16:1301, 1933.
10. Bradbury, S. and Eggleston, C.: Postural Hypotension: Report of Three Cases. Amer Heart J 1:73, 1925.
11. Thomas, J. E. and Schirger, A.: Neurologic Manifestations in Idiopathic Orthostatic Hypotension. Arch Neurol 8:204, 1963.
12. Luft, R. and von Euler, U. S.: Two Cases of Postural Hypotension Showing a Deficiency in Release of Norepinephrine and Epinephrine. J Clin Invest 32:1065, 1953.
13. Hickler, R. B.: Plasma Catecholamine and Electroencephalographic Responses to Acute Postural Change. Amer J Med 26:410, 1959.
14. Rowe, J. C. and White, P. D.: Complete Heart Block: A Followup Study. Ann Intern Med 49:260, 1958.
15. Cowper, W.: Ossifications in the Coats of the Arteries. Philos Tran (abridged) 5:341, 1721.

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In science the credit goes to the man who convinces the world, not to the man to whom the idea first occurs.—Osler



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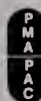
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Neurological Conference

Mental Retardation Associated with Epilepsy*

Doctor David Cannom:**

The patient is a 28-year-old, white, single woman who presently lives with her elderly mother.

Past History

She had been the product of a normal pregnancy and delivery and had remained in good health until age 5½ when she had a febrile illness accompanied by convulsions. She was taken to the hospital where she presented with hemiataxia and bilateral choked discs. Although a craniotomy was performed for a suspected brain abscess, nothing was found. Because the patient subsequently improved clinically, no further operative procedures were undertaken in spite of the fact that a postoperative air study had suggested the possibility of a right parietal mass in the area of the brain.

According to the mother, the patient's early normal mental development had been interrupted at the time of this febrile illness. At age seven, frequently recurring grand-mal seizures appeared. Ultimately, fair control of these seizures was obtained with dilantin and phenobarbital. She continued in school through the seventh grade but did very poorly academically.

Present Illness

The patient was first seen at University Hospitals in October 1957 at age 19, for further evaluation of her seizures and was followed in both Neurology and Psychiatry Clinics until March 1958. She was then having approximately 15 psychomotor seizures a month although there were extended intervals when she was seizure-free. Intelligence tests showed her to have a mental age of eight years 10 months (Stanford-Binet) and an I.Q. of 59. Psychiatric therapy was given in an attempt to control her temper tantrums which usually occurred only with her family, but this was not successful. The psychiatrist felt that she would function best doing simple work under supervision.

She was admitted to the hospital in January 1958 in an attempt to obtain

*Neurological Conference held February 23, 1967. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals.

**Student Doctor, University of Minnesota Hospitals.

Continued

better control of her seizures and to definitely rule out the possibility of a space-occupying lesion. An electroencephalogram showed a marked hemispherical abnormality on the right, but a pneumoencephalogram was unremarkable. Following discharge on dilantin and mebaral, the patient was committed to the Cambridge State School and Hospital in March 1958 by her local probate court. During this period her seizures were well controlled.

Progress

In May 1964 trial placement at the St. Cloud Nursing Home was attempted, but after 10 months she was discharged home. Although trained in dietary areas within the hospital, she had worked as a nurse's aide in St. Cloud.

She was again seen at University Hospitals in June 1966, since her seizures had become more frequent. These seizures were both grand-mal and focal motor in type. An increase in anticonvulsant medication failed to significantly reduce the number of attacks. In December 1966 she fell during a seizure and sustained a fracture of the left knee. Again in March 1967 she fell during a seizure and received a laceration requiring eight stitches above her left eye. A month later she sustained a black eye after a fall.

At the present time she is having approximately one to two grand-mal seizures a week and many more transient psychomotor seizures.

A recent electroencephalogram was moderately abnormal, showing hemispherical asymmetry with slowing over the left temporal area. There were isolated spikes, runs of spikes, and spike-wave complexes predominantly to the right of the central vertex. At times more active spiking was present in the left posterior temporal area. Her present medications include dilantin 400 mg. daily, mebaral 200 mg. daily, and mysoline 500 mg. daily. Of late, she has become quite ataxic, possibly due to the dilantin.

The patient's family relationships have deteriorated in the past few months. She has had frequent fights with her mother and on one occasion threw kitchen objects at her. Her mother is afraid of her and admits to being unable to control her. The patient spends her day watching television and doing a few household chores, with essentially no interests outside the home.

Neurological Evaluation

Dr. Robert Soll:*

According to the history, her original episode was probably an infectious process or similar diffuse inflammatory involvement of the brain. An acute encephalitis of viral origin or an encephalomyelitis could produce extensive damage. After recovering from the acute illness, she had changed both in personality and intelligence. In addition she became plagued by frequent seizures. Throughout the years there has been no significant change in her general condition, and it will probably continue to remain static for the rest of her life without any hope for further improvement.

Progress

Prognostically, complete control of her seizures would be difficult to attain in view of her past history of recurrent seizures despite medication. Since there have been brief periods outside the home when she apparently has been seizure-free, reasonably good control may be possible; factors such as poor

*Neurologist, University of Minnesota Hospitals.

interpersonal relationships at home and unreliability in taking her medications could have contributed to her failure to remain seizure-free.

Treatment

In treating this patient an attempt should be made to secure stable living conditions free of anxiety. Her daily life should have regularity and some supervision, particularly for the medications. Another immediate situation which requires attention is her ataxia. In most situations, a period of hospitalization would help to resolve the question of whether drug intoxication or a progressive lesion were causing the disturbance. Since the patient's original illness was accompanied by ataxia, one might surmise that cerebellar damage was incurred at that time, thus reducing her tolerance to dilantin. In this light, amounts usually considered safe in the average adult might actually be toxic for this patient. Since she has had several falls recently, striking her head, the possibility of a chronic subdural hematoma should also be considered.

Psychological Evaluation

Miss Susan Goodman:*

The patient came readily to the test situation and was friendly, cooperative and chatty throughout. She became quite involved in the procedures and seemed concerned about performing at her best. Although she sought frequent reassurance from the examiner, she appeared to evaluate her capabilities realistically. Her pleasure at unexpected successes resembled the reaction of a child. Although her approach to problem solving was not very systematic, when her attention was directed to the right aspect of a problem, performance often was improved. In this situation she showed none of the hostility and temper described as typical of her behavior at home.

Present test results corroborate the results of tests given 10 years ago in which the patient performed at the mentally defective level. Although the present test results show no evidence of deterioration, it appears that the patient is presently functioning at the upper limit of her capacity. Information obtained from the patient's mother on the Vineland Scale of Social Maturity indicates that she would be incapable of independent self-support and would indeed have difficulty in caring for herself.

Dr. John Brantner:**

It is very interesting that both Miss Goodman and the psychologist 10 years ago noted the evenness of temper, pleasant disposition, and failure to become upset when she was frustrated with anything that she couldn't do. Yet on both occasions the problem for which she was referred was difficulty in controlling her behavior at home.

Social Service Evaluation

Mrs. Janet Johnston:†

Environmentally, the patient's family stems from a rural background. There are eight brothers and sisters, one of whom died of Hodgkin's disease. Since the father's death last year, the mother has maintained a close relationship with the married children, particularly one of the daughters. The

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**Associate Professor, Clinical Psychology, University of Minnesota Hospitals.

†Social Service Department, University of Minnesota Hospitals.

Continued

financial picture involves income from the mother's Social Security of \$81.00 per month and \$20.00 a month from a roomer in her home; the patient herself receives \$67.00 a month Social Security. Interestingly, the mother told me several times that her daughter had had no seizures during her six years at Cambridge. The patient's routine at home involves mostly watching television. She occasionally dries dishes and sometimes tries to read TV magazines but has trouble with the words.

The current trouble according to the mother includes both seizures and uncontrolled temper outbursts, which appear to be unrelated to each other. Her temper outbursts consist of screaming, shouting, and throwing things. Some of the incidents that cause her to become angry are either her mother's difficulty in hearing or her failure to understand. Also she accuses her mother of being partial to the other siblings, and there is a tendency for her to be suspicious of people. The patient declared emphatically that she never wants to return to Cambridge. One has the impression that she is attempting to control her mother by means of the temper tantrums. Unfortunately the home environment is not well enough designed to provide adequate control of the patient.

Mrs. Kathryn Wilcox:*

While the father was still living, the patient, being the youngest child, was closely attached to him. When she wanted her way, all she had to do was throw a temper tantrum, and eventually this became a pattern. After she was released from Cambridge, the father was in favor of the patient coming home but the mother was not. Subsequently, the patient was directed into a rehabilitation program and placed in a St. Cloud nursing home. Although she had been trained as a kitchen and dining room helper, she was employed as a nurse's aide at St. Cloud, which may account in part for her inability to be successful in this program.

Dr. Soll:

What are her feelings towards Cambridge now? She said that she never wanted to return there.

Mrs. Wilcox:

She has not really said why. I told her she would never have to worry about that because it was no longer in our district. She expressed a willingness to try Faribault, however.

Dr. Brantner:

It is interesting that the Cambridge commitment was for seizures, whereas commitment now to Faribault is for behavioral reasons.

Mrs. Wilcox:

Originally, this probably should have been a commitment for mental deficiency; however, it was actually epilepsy. This was a problem within our court.

Dr. Brantner:

Is the patient still under commitment?

Mrs. Wilcox:

Yes. There will be no change in commitment. Faribault now accepts voluntary patients, the only problem being space. It is much easier for them to take

*Case worker from Dodge County Welfare Department.

in a patient such as this one, who does not need much care.

Dr. Brantner:

Also I think it could be pointed out to them that not only would she not need much care, but that with her working history at Cambridge she might make a contribution in the kitchen.

Mrs. Wilcox:

I talked with one of the officials at the Faribault Institute and mentioned the fact that if the patient were admitted to Faribault, it should be on the basis of a training program in which she would have some type of job away from her family. Hopefully there would be a better setting there. Perhaps even working in another institution would be a possibility; actually Faribault wouldn't be the last resort. The principal goal would be to supply training and an opportunity to obtain routine medication.

Dr. Brantner:

That is another thing that should be stressed again. According to her psychological evaluation she is not capable of responsibly managing a complicated medication schedule—even a simple one. I would be suspicious of dilantin toxicity, because patients like her are quite capable of forgetting their medication and then having a grand-mal seizure. Afterwards they remember and take yesterday's, today's and tomorrow's medication all at once.

Mrs. Wilcox:

I told the patient that she should take the medications as they are prescribed, changing only with the doctor's orders. She replied that she always asks her mother if she should change it. So she may not be taking the medications as they are set up. This is part of the problem. Another problem is that the roomer in their house is an older brother of the patient and they do not get along well together.

Discussion With Patient's Mother

Dr. Soll: (to the mother)

We have been discussing the problems you are having with your daughter. How do you feel about the situation as it has developed throughout the years?

Mother:

There doesn't seem to be any future for her at home. I thought her seizures might be controlled better. They were for a while, but they came back again.

Dr. Soll:

It is possible that this has something to do with her environment. How do you feel about her remaining at home or going to Faribault?

Mother:

What sort of an institution is that?

Dr. Soll:

There are several places that take care of the patients who have seizures, and the most logical one for her at present would be a hospital like Faribault. There would be several advantages; for example, there are other patients who have similar problems, so she might develop a sense of belonging rather than being different. Also she would receive her medications regularly.

Continued

Mother:

Would they be able to teach her something?

Dr. Soll:

This is another reason for her going there. Mrs. Wilcox said the understanding would be that she definitely be given a training period to develop any talent she might have. Dr. Brantner brought out the point that she already had training in working in the kitchen at Cambridge. This fact plus the fact that she is independent as far as her own self care is concerned would be an asset for the hospital.

Dr. Brantner:

How did you get along when she was not at home with you? Did you miss her?

Mother:

I was kept busy, because I wasn't alone then.

Dr. Brantner:

Did you visit her frequently?

Mother:

Maybe about once every two months.

Dr. Brantner:

Do you think that she missed you while she was in Cambridge?

Mother:

She was always glad to see us, but I really think that, in a way, she was happier there than she is at home. Of course, she wouldn't admit that.

Dr. Brantner:

No, but there is the problem of her temper. Did she show this in Cambridge?

Mother:

I don't know. I know she had one tantrum, but that is the only one that I know of.

Dr. Soll:

Does she take care of most of her medicines now or do you help?

Mother:

No, I give them to her in the morning.

Dr. Soll:

Has she ever taken more medicine than she should?

Mother:

About a month ago she did happen to take a double dose when she went to bed, not intentionally.

Discussion With Patient and Her Mother

Dr. Soll: (to the patient)

How do you feel about living away from home?

Patient:

It would be better to get out and work again, maybe do more things or something. Now I just sit around. There is not much to do. It's just a little town that we live in, that kind of gets on your nerves too.

Dr. Soll:

Do you ever lose your temper?

Patient:

Yes. I probably lose it sometimes when I shouldn't.

(The patient and her mother leave the conference room.)

Mrs. Wilcox:

The mother probably will feel bad, but hospitalization is for the patient's benefit. The mother finds it difficult to express herself.

Dr. Brantner:

The patient says very clearly that she would like to leave home.

Mrs. Wilcox:

After admission to the hospital her medications will be controlled and she will be placed on the training program they have in that institution (Faribault) or then another institution.

Dr. Soll:

It probably would be best to admit her to the neurology ward at the University for a couple of weeks to correct this unsteadiness.

Dr. Brantner:

It will be better for her to be in an institution, for she will never be self-supporting. She will always need some type of institutional care.

The Management

The recommendations of this conference were as follows:

1. The patient should be admitted to the Faribault State Hospital. It was thought that this decision would both alleviate the tensions between the patient and her mother at home as well as give the patient some vocational training and a sense of personal fulfillment while being a contributing member to the hospital community.

2. Before any final decisions are made it was recommended that the patient be admitted to the University Neurology Service both to evaluate the ataxia and to reassure ourselves that she did not incur any injury during her recent falls.

Robert Soll, M.D.
University of Minnesota Hospitals

Participating in the conference were: Dr. Robert Soll, Neurologist; Student Doctor David Cannom; Miss Susan Goodman, Clinical Psychology Trainee; Dr. John Brantner, Associate Professor, Clinical Psychology; Mrs. Janet Johnston, Social Service Department and Mrs. Kathryn Wilcox, case worker from Dodge County Welfare Department.

I do not greatly care whether I have been right or wrong on any point, but I care a good deal about knowing which of the two I have been.—Samuel Butler

I have always considered that the substitution of the internal combustion engine for the horse marked a very gloomy milestone in the progress of mankind.

Winston Churchill, 1944

Continuation Course in Neurological Emergencies November 8-10, 1967

A continuation course in Neurological Emergencies will be presented by the University of Minnesota from November 8 to 10, 1967, at the Nolte Center for Continuing Education. This course is designed to present material concerning emergencies of the neurological system and the diagnostic and therapeutic methods of managing them. The program is listed below.

Guest speakers will be DOCTORS DAVID D. DALY, Professor and Chairman, Department of Neurology, University of Texas, Southwestern Medical School, Dallas, Texas; and THOMAS R. H. JOHNS, Professor of Neurology, University of Virginia School of Medicine, Charlottesville, Virginia.

The course will be presented under the direction of DOCTORS A. B. BAKER, Professor and Director, Division of Neurology; and ROBERT W. SOLL, Instructor, Division of Neurology. The remainder of the faculty will include members of the faculties of the University of Minnesota Medical School and the Mayo Graduate School of Medicine.

Wednesday, November 8

Acute Spinal Cord Compression

8:55- 9:00 Introduction Fred E. Berger,
Albert Sullivan, Jr.

Chairman: Robert W. Soll

9:00- 9:45 Traumatic Fracture—Dislocation of Verte-
brae Shelley N. Chou
9:45-10:30 Centrally Herniated Discs... Alfred Uihlein
10:45-11:30 Spinal Cord Compression Due to Neoplasm
Donlin M. Long

Infections and Electrolyte Disturbances

Chairman: A. B. Baker

1:30- 2:00 Purulent Meningitis .. Thomas R. H. Johns
2:00- 2:30 Encephalitis and Post Infectious Encephalo-
myelitis Michael E. Blaw
2:30- 3:00 Acute Syndromes Secondary to Major Elec-
trolyte and Water Disturbances John
A. Logothetis
3:15- 3:45 Sinus Thrombosis and Brain Abscess.
Zondal R. Miller

3:45- 4:15 Tetanus A. B. Baker
Thursday, November 9

Bulbar Palsy

Chairman: Harold H. Noran

9:00- 9:30 Poliomyelitis Harold H. Noran
9:30-10:00 Pseudobulbar Palsy George C. Flora
10:00-10:30 Myasthenia William R. Kennedy
10:45-11:30 Guillain-Barré Syndrome David Daly

Stupor and Coma

Chairman: Milton Alter

1:30- 2:00 Examination of the Unconscious Patient
Milton Alter
2:00- 2:30 Acute Intoxications. Edward Jimenez-Pabon
2:30- 3:00 Extradural and Subdural Hematoma .. Ross
H. Miller
3:15- 4:00 Coma Due to Metabolic and Endocrine
Disorders Thomas R. H. Johns

Friday, November 10

Increased Intracranial Pressure and Visual Loss

Chairman: Sidney K. Shapiro

9:00- 9:30 Brain Stem Herniation. William E. Bradley
9:30-10:00 Optic Neuritis James A. Moriarty
10:00-10:30 Rapid Visual Loss Associated with Intra-
cranial Disease Robert J. Goldberg
10:45-11:30 Cerebral Edema and Benign Intracranial
Hypertension Anna L. Ellington

Cerebrovascular Disease and Convulsive Disorders

Chairman: Fernando Torres

1:30- 2:00 Acute Completed Strokes Clark H.
Millikan
2:00- 2:30 Internal Carotid Insufficiency William
J. Riley
2:30- 3:00 Basilar Vertebral Insufficiency Arthur
C. Klassen
3:15- 3:45 Grand Mal Seizures Fernando Torres
3:45- 4:15 Status Epilepticus David Daly

The Barber's Pole

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—Marion Rawson: Handwrought Ancestors

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Clinical Path Conference

Dyspnea and Acute Pneumonic Infiltration

Dr. Robert L. Strom:*

Case Report

A 67-year-old white male was hospitalized at Hennepin County General Hospital because of dyspnea. An emergency room chest x-ray 18 months previously had been interpreted as showing generalized pulmonary fibrosis. Six months previously he had been hospitalized elsewhere and an extensive pulmonary evaluation had confirmed the diagnosis of idiopathic pulmonary fibrosis. Multiple sputum cultures for tuberculosis and fungi showed no growth. A complement fixation test for histoplasmosis showed no titer. Sputum smears for malignant cells were negative.

On admission to Hennepin County General Hospital his dyspnea was so severe that his activity was limited to bed rest. A persistent cough was productive of a cup of white to creamy sputum per day. He was unable to lie flat because of shortness of breath. Hemoptysis, chest pain, chills, fever and edema were specifically denied.

The patient had been hospitalized two years previously with anterior septal myocardial infarction and had required digitalis and aminophyllin since that time. There was a history of heavy cigarette smoking for many years; however, alcohol had been used only in moderation.

Physical Examination

Physical examination revealed: temperature 98.6°F., pulse 140 per minute, blood pressure 130/90, and respirations 40/min. The patient was markedly dyspneic at rest and cyanotic; his neck veins were not distended. The chest had an increased anterior posterior diameter and showed poor expansion with deep inspiration. Both lung bases were dull to percussion, though rales were audible bilaterally to midscapular level. The breath sounds and heart sounds were distant. There was marked clubbing of the fingers and toes and advanced body wasting. The liver was palpable two fingerbreadths below the costal margin.

Physical and Laboratory Studies

The circulation time (arm to tongue) was 16 seconds and the venous pressure, 11 cm. of saline. A measured vital capacity was 1000 cc. total with 700 cc. expired in one second.

Laboratory studies included a hemoglobin of 15.1 Gm. per 100 ml., a white blood cell count of 10,200 mm³ with 84% neutrophils. The urinalysis was normal. An erythrocyte sedimentation rate (Westergren) was 18 mm. per hour and the prothrombin time 13.7 seconds. A fasting blood sugar was 128 mg. %, BUN 11 mg. %, serum sodium 135 mEq/L, potassium 5 mEq/L, CO₂ combining power 30 mEq/L and chloride 98 mEq/L. Cultures of the sputum showed a mixed flora, and two sputum smears for malignant cells were negative.

*Associate Pathologist, Hennepin County General Hospital.

Continued

A chest x-ray showed a bilateral dense pneumonic infiltration with some superimposed pneumonia. The patient remained afebrile the first few hospital days although rales and cyanosis persisted. On the sixth hospital day, increased respiratory distress was noted; the patient became cyanotic and apneic.

Treatment

Treatment included intermittent positive pressure breathing, aminophyllin 250 mg., librium 10 mg., and Keflin 4 Gm. daily. The blood pressure was maintained with Isuprel and solu-cortef. An electrocardiogram showed paroxysmal atrial tachycardia with a variable block. Cardioversion was accomplished and a tracheostomy performed. Isoniazid 100 mg. t.i.d. and para-aminosalicylic acid 2 Gm. q.6.h. were initiated.

On the seventh hospital day the $p\text{CO}_2$ was 45 mm.Hg., and the bicarbonate 36 mEq/L. By the 15th hospital day, the respiratory rate was 65 per minute. The patient suddenly expired shortly after receiving aminophyllin 150 mg. intravenously.

Discussion

Dr. Thomas Lowry:*

I feel very fortunate in having looked at the chest x-rays of this patient, since the protocol does not reflect the severity of the pneumonic infiltration. Throughout the whole story dyspnea is the predominant symptom. In spite of all attempts at supportive measures, the dyspnea was rapidly progressive. The protocol states that he was short of breath for at least six months. On the other hand, he was seen at the Emergency Room approximately 18 months earlier in March 1965 and had a chest x-ray taken. There is no information as to his symptomatology at that time. On his previous hospitalizations he had been fairly well studied and was dismissed with a diagnosis of idiopathic pulmonary fibrosis.

Inhalants

I think whenever you see someone with pretty diffuse fibrosis in the lungs, you would like to know something about his previous occupation. Nothing is said about it and I assume he was not exposed to such things as asbestos, silica, beryllium and the other inhalants that are known to produce an x-ray picture of diffuse fibrosis. The patient arrived here in early December and lived approximately two weeks. During this time he was never well enough for a proper medical evaluation. If he had had some planograms to really shoot through the pneumonic density, we might have a better idea what there was there. Nonetheless, this man was critically ill and remained so in spite of what was done for him.

Significant Negative Findings

His major complaints on this admission were dyspnea and productive cough. There were several important negative findings. He was said very definitely to have no fever, chills, or hemoptysis. With this much disease in his lung, I consider those findings a little surprising; but nevertheless there they are. He was unable to lie flat because of shortness of breath. I think with that much lung disease, one cannot interpret orthopnea as indicative of left heart failure. The patient needs all the mechanical advantage that he can get in the use of his accessory muscles in breathing.

The physical findings which appear to me to be of importance are the tremendously rapid pulse and respiration with a normal blood pressure. The absence of heart failure is notable. Dullness at his lung bases could have been signs of fluid or atelectasis. The rales over his lower lungs fit with the large amount of white or creamy sputum produced.

*Consultant in Internal Medicine, Hennepin County General Hospital.

Restrictive Respiratory Difficulty

The venous pressure and circulation time confirm the absence of heart failure. The vital capacity readings total was 1000 cc. and the one second was 700 cc. If you figure this out mathematically and allow the patient half a second to inhale, he cannot possibly breathe out more than 700 cc. in one second. I think we have to assume that most of his respiratory difficulty was restrictive rather than obstructive. There were no wheezes or evidence that he was having much trouble getting breath out.

The usual laboratory findings are not particularly helpful here. I am going to disregard the blood sugar of 128 mg.% because I do not believe it fits with anything else. The CO₂ combining power and serum bicarbonate are considerably elevated with a high normal pH. We can assume that he was hypoxic, but no oxygen determination was made.

Dr. S. H. Tsai:*

Perhaps we should start with the first x-ray in March of 1965 (Figure 1). At that time there was an area of infiltration with some fibrous strands in the left upper lobe in addition to some very fine nodulation in the right and left lower lung fields. This was the beginning of the disease process. The heart also appears enlarged. Then after a year and nine-month interval in December

*Chief of Radiology, Hennepin County General Hospital.



Fig. 1—Chest roentgenogram of March 1965 with nodular infiltrate (arrow) in left upper lung field.

Continued

1966 (Figure 2) we have very extensive consolidation of both the upper and mid lung fields. We do not see the right upper lobe take-off or the left main stem bronchus. On serial films the heavy bilateral infiltration persisted until the time of his death in mid-December with only minimal variation due to exposure technique.

Dr. Lowry:

The patient received various antibiotics without any apparent improvement, and shortly after that he was placed on steroids and isoniazid. I would assume that the isoniazid was used strictly as a protective measure and not because anyone thought he had tuberculosis. The rapid course appears incompatible with the diagnosis of tuberculosis. After his tracheostomy he had assisted respirations for the remainder of his life. During part of that time his respiratory rate was 65 and all I can say is that my hat is off to anyone who can make a Bird respirator coincide with that rapid a respiratory rate in a patient. My hunch would be that the patient was fighting the Bird respirator as much as he was getting any help from it. I do not think you can assist respiration with a tracheostomy tube when the patient is already breathing 65 per minute.

I am not going to ask to see the electrocardiograms. He is said to have had a myocardial infarction, and this probably accounts for his slight cardiac enlargement. He had a bout of arrhythmia which was controlled without too much difficulty. I cannot ascribe any particular significance to his expiring



Fig. 2—Chest roentgenogram of December 1966 with diffuse pneumonic infiltrate.

while receiving aminophyllin. I think he simply ran out of breathing space and died.

Differential Diagnosis

Now, what are the likely causes of this illness? First of all, I would like to postulate that this man developed something new between 1965 and 1966. I do not think it was the same disease as before unless the small infiltrate in the left upper lobe is an early bronchogenic carcinoma which extended to involve the left mainstem bronchus and part of the right bronchus. I think he had something new, which had to be malignant. The course was much too rapid for other disease processes. His respiratory impairment appears primarily restrictive. *Progressive fibrosis and emphysema* should have advanced much more slowly than this and should theoretically have produced some right heart failure during the terminal course. In this instance the lungs were simply filled up until he had nothing left with which to breathe. I think that *pneumonia superimposed on pulmonary fibrosis* is an untenable diagnosis. He had no fever or significant response to antibiotic treatment. I considered some of the more exotic conditions. The disease course of *sarcoidosis* or the *Hamman-Rich syndrome* does not progress this rapidly. *Wegner's granulomatosis* is unlikely in the absence of upper respiratory granulomas or multi-system disease. Alveolar proteinosis would have run a slower course and been less malignant and rapid in its final conclusion. I have to say in closing that this was an inexorable, rapid and lethal obliteration of pulmonary air space and had to be some type of cancer. The appearance is perfectly compatible with an alveolar cell carcinoma which often has a multicentric origin and a variable x-ray picture. Usually, however, the course of that disease is not this rapid. I am more impressed with the possibility that this was a bronchogenic carcinoma that spread along the bronchi and closed them off until finally the airway was obliterated.

Clinical diagnosis:

1. Bronchogenic carcinoma of the lung with hilar involvement.
2. Healed myocardial infarction with cardiomegaly.

Pathology

Dr. Strom:

Cardiac Findings

Since the lung was the area of major interest, I will leave that to the last and comment on some of the other post-mortem findings. On opening the chest cavity, the pericardial sac was obliterated with fibrous adhesions. These were nonconstricting and were likely related to his previous myocardial infarction. His heart weight was 420 grams and there was occlusion of the left anterior descending branch of the coronary artery with an old anterior septal myocardial infarction involving the subendocardial region.

Intraperitoneal Findings

The liver showed changes of passive congestion and there was a small recent splenic infarction. Two depressed scars were present in the cortical portions of the right kidney, perhaps related to an embolic phenomenon during the myocardial infarction two years previously. The gastrointestinal tract was

Continued

entirely normal throughout. I think this is important, because we searched the gastrointestinal tract very closely in this case for possible gastrointestinal primary malignancy.

Pulmonary Findings

The process in the lungs held our major interest. The lungs were exceedingly heavy, with considerable fibrotic peel over their surfaces. I believe the degree of pleural thickening might have contributed to the extensive pulmonary x-ray findings. Both lungs were firm to palpation, and the apices were relatively spared of the process as opposed to the more dependent portions of the lungs. The cut surface of the lung showed multiple yellow-white mucoid tumor nodules and infiltrations, some of which had a lobar distribution. However, in the left apical posterior segment there was a 2½ cm. confluent necrotic mass. The localized nodule on the chest x-ray in 1965 would likely conform to this density in the left upper lobe. It is very difficult at times to differentiate between a peripheral bronchogenic adenocarcinoma and a terminal bronchiolar carcinoma or alveolar cell carcinoma. In this instance there were no distinct metastases to other organs and no evidence of tumor in the hilar lymph nodes, although the nodes were somewhat enlarged. Therefore we prefer to classify this as a case of alveolar cell carcinoma or terminal bronchiolar carcinoma with widespread lobar involvement. Heavy mucous plugs were present in the tracheobronchial tree, and there may have been some terminal acute bronchitis as well.

The histology of the tumor nodules is rather interesting in that the histologic cell type is the mature columnar mucus-secreting cell. This is an unusual pattern for alveolar cell carcinoma. The microscopic picture in Figure 3 is characteristic of a mucus-producing alveolar cell carcinoma. The general topography suggests that the mucus-secreting epithelium was laid down around the periphery of the alveolus itself and perhaps did not disrupt the terminal alveolar structure too significantly. Such tall columnar epithelium is much more frequently observed in metastatic carcinomas, particularly from the gastrointestinal tract. Carcinoma of the colon or an occult primary in the

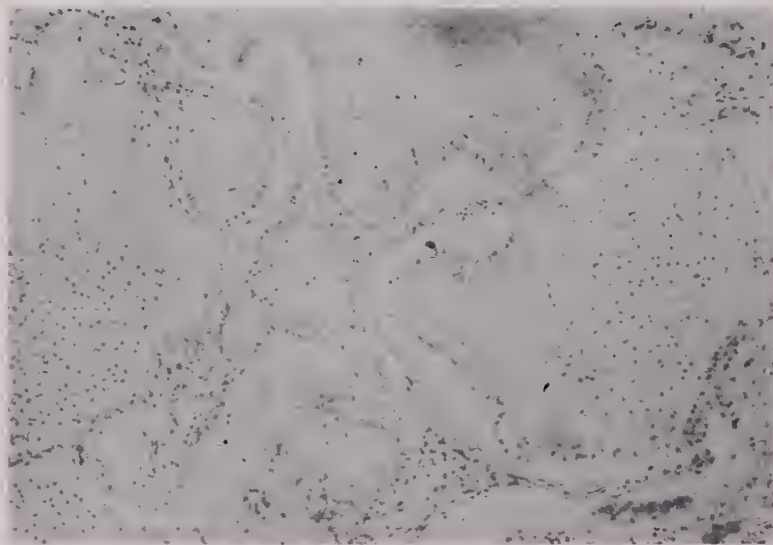


Fig. 3—Alveolar cell carcinoma of the lung. Note tall columnar mucous-secreting epithelium lining alveolar spaces.

stomach can metastasize to the lungs and give this histologic appearance. For this reason, we studied the stomach very closely and were unable to demonstrate a primary lesion in the gastrointestinal tract.

Retrospective Findings

I went back and reviewed the sputum cytologies on this patient to see if we had missed something. It is said that alveolar cell carcinoma is easily diagnosed on sputum cytology. Frequently the pulmonary cytology of alveolar cell carcinoma reveals clumps of uniform sized cells with an altered nuclear cytoplasmic ratio and rounded dark chromatin with prominent nucleoli. It is more unusual when an alveolar cell carcinoma presents with a mucus-secreting tall columnar type of epithelium such as we have seen in this case. In reviewing this patient's sputum, I felt the cytology was rather poorly preserved. Many macrophage* type cells were observed together with some tall columnar type epithelium. As you can see (Figure 3), this is a rather mature type of bronchial epithelium similar to that seen in inflammatory conditions of the bronchi. The degree of fibrosis within the lung parenchyma itself does not suggest that this could be a Hamman-Rich syndrome with epithelial proliferation. I think the findings are quite consistent with a mucus-producing type of alveolar cell carcinoma of the lung.

Anatomic diagnosis:

1. Mucus-producing alveolar cell carcinoma of the lungs.
2. Old myocardial infarction.
3. Cardiomegaly and adhesive pericarditis.
4. Old renal infarctions.
5. Recent infarct of the spleen.

Dr. Lowry:

We often think of carcinoma of the lungs as metastasizing distantly and we often forget that the common site for metastases is the other lung. Metastases of bronchogenic carcinoma to the other lung are by no means infrequent. To me, the clue in this case, and at one point I was certainly looking for it, is the accelerated terminal course.

Dr. Tsai:

Returning to that chest x-ray in March of 1965, I am sure the density in the left upper lobe was the beginning of the disease process, and the fine nodularity was likely tumor cells starting in the alveoli. Dr. Leo Rigler was discussing alveolar cell carcinoma at a recent meeting and showed a series of similar cases with a fibrous band extending into the lesion.

Dr. Strom:

The localized nodule on the x-ray in 1965 would likely conform to the density in the left upper lobe that we observed at autopsy. This was a necrotic nodule which seemed to be a possible focus from which the remainder of the tumor developed.

Robert L. Strom, M.D.
Hennepin County General Hospital

*See Test Your Word Score Page 1513.



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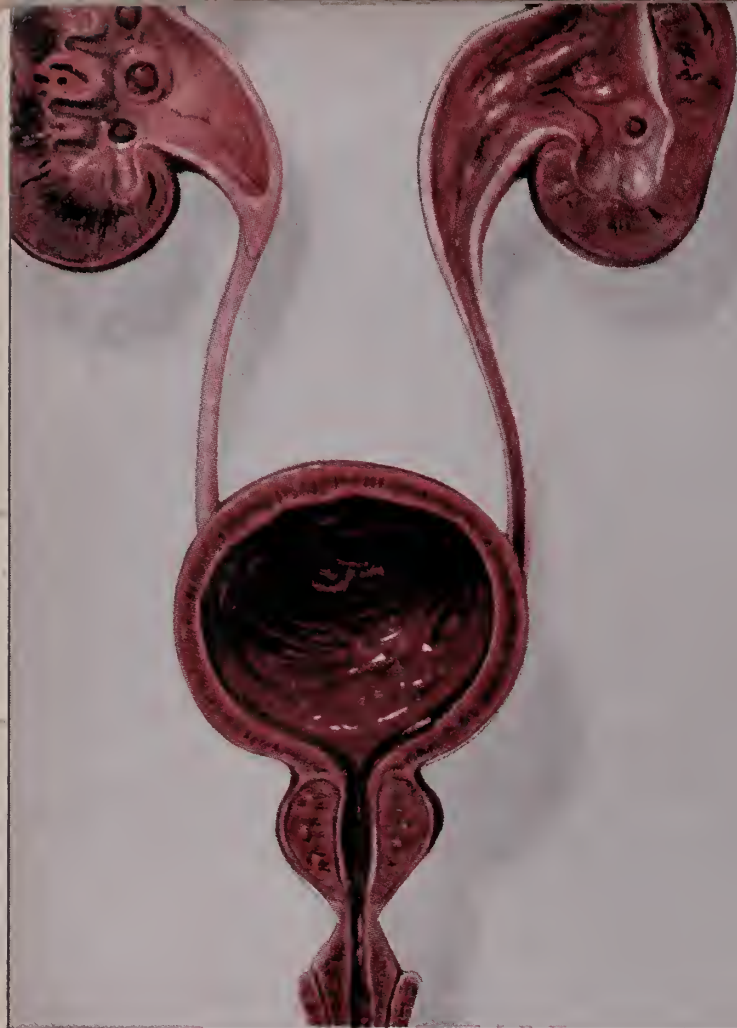
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References: (1) Based on 23 clinical papers, 1512 cases. Bibliography on request. (2) Bush, I. M., Orkin, L. A., and Winter, J. W., in Sylvester, J. C.: Antimicrobial Agents and Chemotherapy—1964, Ann Arbor, American Society for Microbiology, 1965, p. 722.

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Hematopoietic

EOSINOPHILIA is frequently observed, is sometimes pronounced, and can be caused by several, if not all, antimicrobial drugs. On occasion, methicillin, oxacillin, novobiocin, lincomycin, colistin, cephalothin, amphotericin B, and griseofulvin have caused transient leukopenia. Another interesting complication involving the hematopoietic system is the acute, self-limited hemolytic anemia that occurs in certain individuals after the administration of penicillin G, especially when large amounts are given for prolonged periods, as reported by Van Arsdel and Gilliland.²⁰ Certain other individuals in whom acute hemolytic anemia develops have red blood cells that are deficient in the enzyme glucose-6-phosphate dehydrogenase. This biochemical peculiarity is genetically determined, and the defect may remain undetected until such individuals are exposed to one of the oxidant drugs. The sulfonamides, as well as nitrofurantoin, may cause anemia via this mechanism. In this type of anemia hemolysis of the older erythrocytes occurs, whereas the younger erythrocytes remain resistant; hence the acute self-limited course. Survival time of the red cells is reduced to several days, and hemolysis along with reticulocytosis and hemoglobinuria may occur.

The outstanding untoward reaction after therapy with chloramphenicol is, beyond a doubt, bone marrow depression. In a nationwide survey in 1954, a total of 1,167 patients with blood dyscrasias was noted, and 29 of the patients had received chloramphenicol as the sole drug. Of the 29 patients, 17 were less than 10 years of age and

Caucasian girls predominated two to one. Eighty-eight other patients had received chloramphenicol in addition to other drugs. Of the patients with blood dyscrasias in which chloramphenicol was implicated, 68% had aplastic anemia, and most of these patients had received intermittent courses of therapy. An increased incidence of chloramphenicol-induced marrow depression may also occur in patients with hepatic or renal insufficiency. Hematotoxicity is more likely to occur when levels of chloramphenicol in the blood are sustained at 25 µg/ml. or higher. It is variously estimated that the incidence of chloramphenicol-induced aplastic anemia is 1 in 100,000 to 1 in 800,000, with a mortality rate of 50%. Today, with the availability of various effective anti-staphylococcal agents, chloramphenicol probably should not have a routine place in the management of such disease but should be limited to selected gram-negative bacillary infections, especially those due to *Salmonella typhosa*.

Unfortunately, there is no single laboratory procedure that immediately identifies impending chloramphenicol-induced blood dyscrasias. Also, detection of the complication and stopping administration of chloramphenicol may not prevent relentless progression to aplastic anemia. In addition to reticulocytopenia and increased values for serum iron, there are other indices of chloramphenicol's interference with iron metabolism. These include an increase in saturation of iron-binding globulins, a delayed clearance of plasma iron, and a failure of radioactive iron to be incorporated into erythrocytes.

In some cases at least, chloramphenicol-induced suppression of the marrow may represent an accentuated normal response to the drug, because

Continued

*See Part I, Minnesota Med 50:1393, 1967.

mild reversible changes are not rare and large doses given for prolonged periods cause arrest of maturation in most subjects. The metabolic handling of chloramphenicol has been studied in patients who have recovered from chloramphenicol-induced suppression of the marrow; the drug was detoxified and excreted by them in a normal manner. Therefore, hematotoxicity due to chloramphenicol is not invariably a hypersensitivity reaction.

Some data have been interpreted as indicating that L-phenylalanine given orally in amounts of 100 mg/kg. of body weight per day may ameliorate chloramphenicol-induced hematotoxicity, but other workers disagree.²¹

Use of the anabolic drug, oxymetholone, may stimulate regeneration of the bone marrow.

Antimicrobial agents, in addition to chloramphenicol, that may be associated with significant blood dyscrasias are the sulfonamides, ristocetin, and less frequently streptomycin, the tetracyclines, and novobiocin. Methicillin, amphotericin B, and griseofulvin probably have caused marrow depression. The tetracyclines, ristocetin, and amphotericin B may have a special propensity to cause thrombocytopenia in such cases.

It has been mentioned previously that certain antimicrobial agents, especially when the tetracyclines are given intravenously, may interfere with coagulation of blood. In this regard, some data suggest that griseofulvin may alter the anticoagulant activity of warfarin, and consequently, if these two drugs are being administered concomitantly, it is recommended that the prothrombin time be determined frequently, at least initially.

Genitourinary

Antimicrobial-induced renal complications usually present themselves in a similar fashion, despite the drug responsible, and only regular testing will detect them at their onset. The alarm may be given when proteinuria, cylindruria* or microscopic hematuria is found, and the complication may progress to increases in the concentrations of urea and creatinine in the blood. These complications may occur in patients with normal kidneys, although they are more likely to appear earlier in patients who already have decreased renal function. Usually these untoward effects disappear if administration of the offending antimicrobial drug is discontinued sufficiently early.

The potentially nephrotoxic drugs include streptomycin, dihydrostreptomycin, neomycin, kanamycin, amphotericin B, vancomycin, polymyxin B, colistin, and the sulfonamides. Whether ristocetin is nephrotoxic is debatable. It appears increasingly evident that methicillin is nephrotoxic and, rarely, penicillin G has been nephrotoxic, evidently via the mechanism of allergic vasculitis. One should avoid giving excessive doses of paromomycin (Humatin) because the drug is potentially nephrotoxic. Nalidixic acid has resulted in increased azotemia. Increased azotemia also has followed administration of cephalothin, and on occasion the azotemia may be severe enough to be suggestive that in the future the drug may be classed as nephrotoxic. Also, rarely, patients who had normal renal function prior to treatment with cephalothin have experienced azotemia while receiving the drug. Retention of these drugs by previously damaged kidneys may lead to nephrotoxic serum concentrations. Also such factors as dehydration, hypotension, conjoint use of other nephrotoxic drugs, infancy, and advanced age may abet the occurrence of antibiotic-induced nephrotoxicity. From the histologic standpoint, as a generalization, the nephropathies are characterized by necrosis and desquamation of the convoluted tubules, but biopsy has revealed interstitial nephritis in some cases.

Gross,²² as well as Frimpter and associates,²³ reported patients with a reversible type of Fanconi syndrome resulting from ingestion of outdated or degraded tetracyclines. Dehydration, vomiting, muscle weakness, polydipsia, polyuria, glycosuria with a normal blood sugar, metabolic acidosis, proteinuria (sometimes of the Bence Jones type), aminoaciduria, hypokalemia, and hypocalcemia may occur. These complications may be important considerations to any physician who uses professional samples for his personal use.

Castell and Sparks²⁴ described an isolated defect of renal tubular function manifested by polyuria and hyposthenuria after ingestion of demethylchlortetracycline (Declomycin); this example of so-called nephrogenic diabetes insipidus appears to be a reversible effect of the intact drug and unrelated to excessive dosage. The tetracyclines, via their antianabolic effect in patients with underlying renal disease, may increase the degree of azotemia. These drugs may also ad-

*See Test Your Word Score Page 1513.

versely affect the kidneys via the "hepatorenal syndrome" in patients in whom the drugs have caused hepatotoxicity.

As noted under respiratory reactions, certain organisms, such as *Pseudomonas*, are referred to as "water bacilli," indicating their frequent presence in various fluids and on medical instruments exposed to fluids. This residence in solutions explains some iatrogenic urinary infections, in which the urologist inadvertently introduces fluids laden with *Pseudomonas* into the patient's bladder during cystoscopy and allied procedures. As previously noted, infection with these "water bacilli" is abetted if the patient is receiving an agent, such as a penicillin, to which the organisms are resistant.

When a tetracycline is added to solutions employed in peritoneal dialysis, the possibility of an untoward effect of the antibiotic should be considered. In markedly azotemic patients, levels in serum may approach the therapeutic range within 15 to 20 hours.

Gross hematuria is rarely an untoward reaction associated with antimicrobial therapy, but it has occurred on administration of the sulfonamides, chloramphenicol, and ristocetin.

During pregnancy, one should be reticent to employ the tetracyclines because of possible untoward reactions, both in the mother and in the newborn baby. As aforementioned, the tetracyclines can cause serious hepatotoxicity in pregnant women.

Administration of a tetracycline during odontogenesis may be associated with discoloration and hypoplasia of primary and secondary teeth, the degree of discoloration being related to the dose. Apparently the drug is incorporated in the enamel as a calcium orthophosphate complex and changes slowly from an ultraviolet fluorescing bright yellow to a non-ultraviolet fluorescing brown.²⁵ Because of these findings, one should be cautious in prescribing these drugs for pregnant women, as well as for children less than four years of age.

Because of their affinity for mineralized tissues, the tetracyclines interfere with the intra-uterine growth of long bones in experimental animals. Via fluorometry, transplacental deposits of the tetracyclines have been noted throughout the human fetal skeleton; in these cases, there is reversible depression of skeletal growth on short-term administration of the drugs.

The possibility of cataract formation in infants of mothers given a tetracycline during pregnancy or breast feeding is suggested but awaits confirmation.

Streptomycin and kanamycin should be used cautiously in pregnant women for fear of inducing ototoxicity in the infant.

Gynecomastia and pigmentation of the genitalia may occur on use of griseofulvin.

Vaginitis or pruritus vaginae may complicate therapy with certain antimicrobial drugs, including use of a tetracycline or lincomycin.

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References

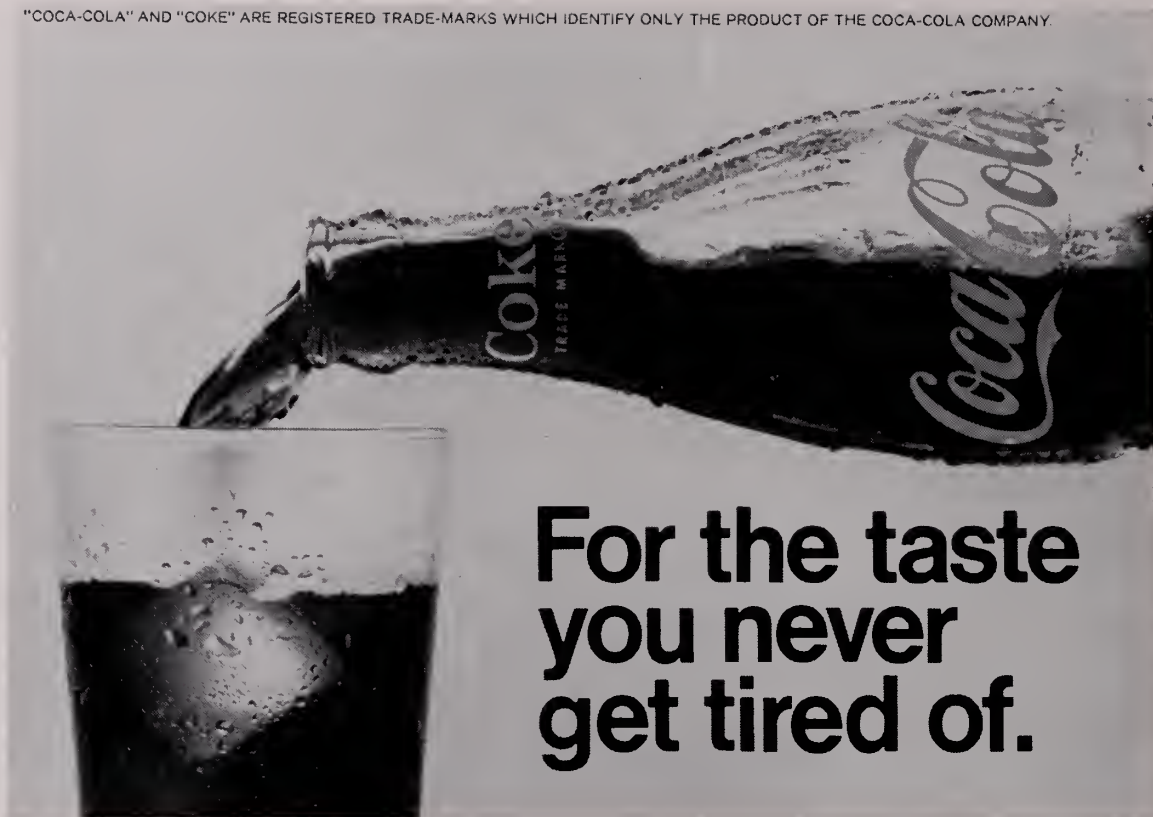
1. Martin, W. J.: Complications of Antibiotic Therapy in the Management of Bacterial Infections. *J Lancet* 86:159, 1966.
2. Martin, W. J.: Newer Antimicrobial Agents Having Current or Potential Clinical Application. *Med Clin N Amer* 48:255, 1964.
3. Martin, W. J.: Some Current Concepts in Infectious Diseases. Part VI. Antimicrobial Agents: Untoward Reactions and Clinical Axioms. *Med Ann DC* 33:18; 46, 1964.
4. Martin, W. J., and Wellman, W. E.: Clinical Use of Antimicrobial Agents. In Brennemann, J.: *Practice of Pediatrics*. Hagerstown, Maryland, W. F. Prior Co., 1:44:1, 1963.
5. Martin, W. J., and Wellman, W. E.: Clinically Useful Antimicrobial Agents. 3. Untoward Reactions. *Postgrad Med* 33:327, 1963.
6. Martin, W. J.: *Current Practices in General Medicine*. 18. Clinical Use of Antimicrobial Agents. *Proc Staff Meet, Mayo Clin* 35:593, 1960.
7. Riggs, B. L., Jr., Geraci, J. E., and Prickman, L. E.: Untoward Reactions to Antibiotics. *Minnesota Med* 44:406, 1961.
8. Turck, M., and Petersdorf, R. G.: Untoward Effects of Antimicrobial Therapy. *Northwest Med* 64:665, 1965.

9-25 May be secured from the author or the reprints.

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Grand Rounds

Pernicious Anemia and Myxedema as Coexisting Disease

WILLIAM TORP, M. D.
Medical Resident

THE OCCURANCE of anemia in patients with hypothyroidism has long been known but it is only relatively recently that any basis for this association has been established.

Background

In 1893, Byrom Bramwell, in describing the clinical picture of myxedema, stated: "Some anemia is usually present in myxedema; but the alterations in the blood do not present any notable peculiarities."¹ Apparently there are earlier references to this subject; Tudhope and Wilson cite an article by Charcot which appeared in 1881.² The Mayo Clinic published a study in 1923 of associated diseases in 628 cases of pernicious anemia.³ Seven of these patients had thyroid disease.

Means and his associates are usually cited for first describing the occurrence of pernicious anemia and myxedema although other authors had recognized the resemblance of pernicious anemia to that anemia sometimes found in hypothyroidism.⁴⁻⁹

Sturgis reported an excellent hematologic response to liver extract therapy in one patient with myxedema.⁵ He also noted that while the patient had a BMR of -30 before developing anemia, this became normal when the anemia was most severe and then was again markedly abnormal after correction of the anemia. Sturgis felt that the increased metabolic activity of the processes

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, February 7, 1967.

Continued

of the anemia masked the decrease normally seen in myxedema.

Means et al.⁶ reported five cases of myxedema associated with pernicious anemia in 1931. All of their patients were achlorhydric.* Four had the typical responses to liver extract and thyroid medication that one would expect in pernicious anemia and hypothyroidism. The fifth patient was felt to have both diseases but did not have optimal response to the double therapy.

In 1936, Greene discussed the difficulty one might have in differentiating between these two diseases.⁹ He reported three cases, one of which had pernicious anemia and myxedema and the remaining two had myxedema and also close resemblance to pernicious anemia. He stated: "Clinical manifestations of myxedema and pernicious anemia are sufficiently alike to account for the fact that the former disease is frequently mistaken for the latter."

While this paper is limited to the discussion of pernicious anemia and myxedema occurring together it should be noted that this type of anemia has also been associated with thyrotoxicosis. McNicol, in 1961, published a series of 256 cases of pernicious anemia and a like number of controls.¹⁰ Thirteen of the pernicious anemia patients also had a history of thyrotoxicosis while only two of the controls had such a history.

Frequency

Anemia in hypothyroidism is fairly common. Tudhope published a series of 116 patients with primary hypothyroidism who had not been treated for their disease and reported 37 (32%) of them as having anemia.¹¹ Five of these were normocytic and responded well to thyroid alone, thirteen had pernicious anemia, seventeen had a microcytic anemia which required iron therapy and two had a macrocytic anemia other than pernicious anemia. Holboll, in 1936, reported a decreased hemoglobin ("less than 70%") in 13 of 28 hypothyroid patients.¹² Lerman and Means in 1932 reported anemia in 60% of 52 hypothyroid patients.⁷ Tudhope makes the statement that anemia other than iron or B₁₂ deficiency in these patients is quite uncommon.

The frequency with which clinical pernicious anemia occurs in patients with myxedema has been reported as high as 12.3% in a series of 73 patients reported by Tudhope and Wilson¹³ (See Table 1). Doniach and associates reported two series of patients, each made up of 100 hypothyroid patients.¹⁴ One of these series included two cases of pernicious anemia and the other series had eight cases.

TABLE 1*
Incidence of Pernicious Anemia in Hypothyroidism,
Thyrotoxicosis and the General Population

	Total	P.A.	Incidence P.A. (%)
Hypothyroid			
All cases	166	13	7.8
Spontaneous	97	10	10.3
Post thyroidectomy, 1 ¹³¹	67	3	4.3
Thyrotoxicosis	760	9	1.2
General Population (45 years old and over)	12,639	44	0.35

*Tudhope and Wilson, Quart J Med 29:513, 1960.

*See Test Your Word Score Page 1513.

Common Clinical Findings

An interesting aspect of Tudhope's paper is an observation that has also been made by other investigators. He had 73 patients with primary hypothyroidism, nine of whom had clinically evident pernicious anemia.

Gastric Analysis

Fifty-two patients had gastric analysis and 24 were found to have histamine-fast achlorhydria. (Lerman and Means reported achlorhydria in 53% of hypothyroids.)⁷ Eleven of the achlorhydric patients who did not have pernicious anemia had Schilling tests, and seven of these eleven had urinary excretion of less than 10%. All hypothyroid patients with normal gastric acid had normal Schilling tests.

Serum B₁₂

Tudhope also reported seven patients who had subnormal serum B₁₂ levels but no pernicious anemia. He recommends that any hypothyroid patient with achlorhydria should be thoroughly investigated for pernicious anemia and should continue to be followed since he may develop pernicious anemia. It should be re-emphasized that one of these conditions may mask the other and one must look for the coexisting conditions. Tudhope cites one hypothyroid patient who developed angina while being treated with thyroid; medication was stopped. He was found to have pernicious anemia and was treated with vitamin B₁₂ with good hematological response. When thyroid treatment was resumed the patient no longer had angina.²

Immunologic Basis for the Two Diseases

While the relationship of pernicious anemia and thyroid disease was first suggested by Lerman and Means in 1932, the basis for the relationship was not clear until recently when auto-immune antibodies and techniques to allow their study were discovered and developed.

In 1958, Schwartz found intrinsic factor inhibiting substance in the serum of pernicious anemia patients who had been treated with oral intrinsic factor.¹⁵ They found this substance in 16 of the 21 patients. In 1959, Taylor found intrinsic factor antibody in pernicious anemia patients who had not been treated or who had received parenteral treatment only.¹⁶ Schwartz, in 1960, studied 91 patients with pernicious anemia and found intrinsic factor antibody in 36. He was unable to detect this antibody in the serum of 39 control subjects.¹⁷

TABLE 2*
% Positive Complement Fixation Tests

Diagnosis	No.	Body of Stomach	Thyroid	Liver
Pernicious Anemia	41	75	37	0
Treated (B ₁₂)	14	64	17	
No treatment	27	82	48	
Hypothyroid	77	22	64	4
Hashimoto's	44	29	81	4
Control	100	4	4	0

*Irvine, et al., Brit Med J 2:454, 1962.

Continued

In 1962, Irvine and associates studied patients with pernicious anemia and thyroid disease using complement fixation tests against thyroid and body of the stomach.¹⁸ The two groups of patients cross-reacted as shown in Table 2. It is interesting to note the results of the control subjects and the lack of cross reaction with liver.

Thyroid Antibodies

Thyroid antibodies can be divided into three distinct organ-specific antigen-antibody systems.¹⁹ They all involve normal thyroid constituents and the antibodies migrate with the gamma globulins on electrophoresis. They are: thyroglobulin, a second protein of the acinar colloid, and an antigen in the microsomal fraction of thyroid epithelial cells.

These can be detected by tanned red cell agglutination test, complement fixation, the precipitin test, or immunofluorescence with varying degrees of sensitivity. The tanned red cell agglutination is thought to be the most sensitive of the tests and involves thyroglobulin antibodies. Some time after Irvine demonstrated that 75% of his patients with pernicious anemia gave a positive complement fixation test to a saline extract of gastric mucosa, it was shown by Taylor and by Irvine that the antibody involved was specific for the cytoplasm of the parietal cell.²⁰ More specific methods for detecting intrinsic factor antigen-antibody reactions were also worked out.

In 1962, Markson and Moore studied the incidence of hypothyroidism in 78 pernicious anemia patients, using tests for thyroid antibodies.²¹ One third of the anemia patients had positive results for thyroid antibodies by one of the three tests employed (tanned red cell agglutination, precipitin test or the complement fixation test), while this was true in only 20% of the controls. They felt the tanned red cell agglutination test was the most sensitive of the three tests. In another paper they reported that in patients with pernicious anemia the gastric mucosa antibody was demonstrable in 32%, while complement fixation test for thyroid was positive in 9%. In patients with Hashimoto's disease the gastric mucosa test was positive in 2.5% and the complement fixation test for thyroid antibodies was positive in 74%.²²

Roitt and Doniach studied the incidence of thyroid antibody in normal subjects and in various types of thyroid disease.²³ Using the complement fixation test they were unable to demonstrate any thyroid antibody in 195 controls and, when using the more sensitive tanned red cell agglutination, the test was positive in only ten of 148 controls. On the other hand, in the 101 primary myxedema patients, 83% were positive using one or more tests, and in patients with Hashimoto's thyroiditis 98% had demonstrable circulating antibodies. In further studies with thyroid antibodies these authors report that in a series of pernicious anemia patients who did not show any overt thyroid disease, thyroid antibodies were demonstrable in 45% but in only 13% of controls.²⁴ On the other hand, 83% of patients with pernicious anemia were positive for gastric cytoplasmic antibody, while in Hashimoto's thyroiditis and in thyrotoxicosis the figures were 27% and 33% respectively.

Irvine and associates in 1965 in a preliminary report on the immunological relationship between pernicious anemia and thyroid disease reported a series of 41 cases of pernicious anemia, 75% of which showed antibody against gastric body mucosa and 37%, complement fixing antibody against thyroid.²⁴ In 121 cases of Hashimoto's thyroiditis or primary myxedema, 70% were posi-

tive for complement fixing antibodies against thyroid and 25% showed antibody specific for gastric body mucosa. In a later article Irvine reported that 73% of a group of pernicious anemia patients showed antibody against parietal cells and 55%, antibody to intrinsic factor, while 86% showed either or both of these antibodies.²⁵ It is interesting to note the incidence of antibodies in chronic hypochromic anemia as compared to the controls (Table 3). Other investigators have also made this observation and have suggested that this could be a stage in the process that ultimately results in pernicious anemia.

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TABLE 3*
Incidence of Gastric and Thyroid Antibodies in Patients with Pernicious Anemia and Some Related Disorders

Diagnosis	# Cases	PERCENT POSITIVE			
		Gastric		Thyroid	
		Parietal Cell	Intrinsic Factor	Tanned Cells and/or Comp. Fix	Gastric and/or Thyroid
Pernicious anemia	130	73	55	41	90
Latent pernicious anemia	6	100	50	50	100
Chronic hypochromic anemia	55	14	2	12	20
Thyrotoxicosis	302	24	3	48	57
Chronic thyroiditis	258	30	3	78	85
Blood donors (15-65, male and females)	629	5		13	16

*From Irvine, New Engl J Med 273:432, 1965.

Roitt and Doniach did a comparison study of auto-antibodies in pernicious anemia, Hashimoto's and primary myxedema, systemic lupus erythematosus and a group of hospital controls²⁸ (Table 4). This again tends to bear out the specificity of these antibodies and the very high rate of occurrence of both thyroid and gastric parietal cell antibodies in pernicious anemia and myxedema.

TABLE 4*
Comparison of Auto-Antibodies in Pernicious Anemia, Thyroiditis, SLE and a Control Series

	Pernicious Anemia	Hashimoto's & Primary Myxedema	SLE	Hospital Controls
	189 cases	394 cases	106 cases	
Auto-Antibody				
Gastric parietal cell	89%	32%	2%	2-16%
Thyroid cytoplasmic	55%	87%	2%	0-15%
Anti-nuclear factor	11%	11%	100%	0-19%

*From Roitt, et al., Ann New York Acad Sci 124 Pt II:640, 1965.

Jeffries, in attempting to show the immunologic basis for pernicious anemia, did a very interesting experiment in which he treated one patient with prednisone for four months.²⁹ He felt that if this is an immunologic process he should be able to suppress it with steroids. The patient showed a decrease in titer of serum intrinsic factor antibody, a normal B₁₂ absorption and regeneration of gastric glands. Similar experiments by others have not had such favorable results, however.

The familial aspects of pernicious anemia are well known. Doniach and Roitt, in a study of families of patients with pernicious anemia and thyroiditis,^{30,31} found a much greater occurrence of gastric parietal cell antibodies

Continued

and thyroid antibodies among the relatives of these patients than among a control group.

Summary

In the simultaneous occurrence of myxedema and pernicious anemia there are many common clinical and laboratory manifestations. There is also good evidence for an immunologic relationship. Various workers starting with Means and Lerman have pointed out the more than chance coexistence of these two diseases. Tudhope's series of myxedema patients showed the presence of pernicious anemia in 12% of cases. With the development of immunologic techniques in this area, an even closer relationship between the two diseases was noted.

The point is made by many of the investigators that one of these diseases may mask the presence of the other. For a satisfactory clinical response it is necessary to recognize both diseases.

Case Reports

Case 1

This was the second hospital admission for a 33-year-old female patient who presented with an elevated temperature, chills, fever and some recent complaints compatible with orthostatic hypotension. She had a previous history of treatment for anemia and stated that her father was a pernicious anemia patient. She had received psychiatric treatment in the past for schizophrenic reactions. The patient was chronically constipated and had noted cold intolerance.

Physical Examination

Blood pressure 110/70, pulse 90, temperature 101. She was an icteric-appearing white female, with a flattened affect. Her hair was coarse and straight. The thyroid was easily palpable and soft. There was a low-grade systolic murmur heard best along the left sternal border. The liver was palpable at the right costal margin and the spleen 3 cm. below the left costal margin. The skin was dry. The tendon reflexes showed a slow relaxation phase.

Hospital Course

Hemoglobin on admission was 6.1 Gm. with a wbc. of 2,600 and a platelet count of 40,000. A bone marrow examination was compatible with pernicious anemia. A Schilling test showed less than 1% excretion. (Report of a bone marrow done 13 years previous to this admission stated that there was no evidence of pernicious anemia and was compatible with iron deficiency. Reticulocyte rose to 28% after starting vitamin B₁₂. Serum iron and percent saturation were below normal, while the iron-binding capacity was normal. Protein-bound iodine was 4.6 and 4.2. Radioactive iodine uptake was 10% and after TSH stimulation 17%. Total thyroxin was in the normal range and BMR was +2. Thyroglobulin auto-antibodies were negative. Gastric analysis showed achlorhydria.

It was felt that the patient was clinically hypothyroid as well as iron and vitamin B₁₂ deficient. She was treated with B₁₂ and iron while in the hospital, her hemoglobin rose to 10 Gm., and she was much improved clinically. Her present hemoglobin is 13.1% with hematocrit of 39%. Thyroid extract therapy was begun and monthly vitamin B₁₂ injections continued.

Case 2

This was the first admission for a 69-year-old patient who complained of weakness, fatigue, malaise, anorexia and weight loss along with paresthesias for one to two months prior to admission. His friends had recently told him that his skin looked yellow. He had previously been in good health.

Physical Examination

Blood pressure 114/60, pulse 100 and regular. He was a moderately obese, irritable,

white male, with a yellow skin color. The sclerae were mildly icteric. Funduscopy examination showed a few flame-shaped hemorrhages. The tongue was pale and smooth. There was a soft systolic heart murmur. Abdomen was negative. Neurological examination showed decreased strength in the extremities along with some decrease in vibratory sense.

Hospital Course

The blood on admission showed hemoglobin of 3.6 Gm., 2,300 wbc. Bone marrow was done on the day of admission and the patient was then given two units of packed red blood cells and was digitalized. He tolerated this quite well and felt much better. The bone marrow was compatible with pernicious anemia and increased iron stores were noted. A Schilling test result was 3% excretion, bilirubin 5.1 total, LDH 1010 and cholesterol 50 mg %. The patient was started on vitamin B₁₂ and had a reticulocyte response to 19% although his hemoglobin did not respond optimally and remained at 6 to 7 Gm. The wbc. and platelet counts rapidly returned to normal. There was no response with folic acid. On the twenty-third hospital day oral iron therapy was started after obtaining serum iron studies. Serum iron was 20 micrograms percent and iron-binding capacity was 136 micrograms percent. His hemoglobin then rose to 10.5 Gm. while in the hospital; three months from the date of his admission the hemoglobin was 14.3. Protein-bound iodine was 3 micrograms percent, radioactive iodine uptake was 10% and after TSH stimulation was 13%. It was felt that the patient was hypothyroid and he was started on thyroid extract with rapid improvement of his clinical state. He is now being maintained on 3 Gm. of thyroid extract and doing well. His hematological picture is normal and stable. Antithyroglobulin titers were normal in this patient.

References

1. Bramwell, Byrom. *Edinburgh Med J* 38:985, 1893.
2. Tudhope, G. R., G. M. Wilson. *Quart J Med* 29:513, 1960.
3. Giffin, H. Z., J. P. Bowler. *Minnesota Med* 6:13, 1923.
4. MacKenzie, G. M. *JAMA* 86:462, 1926.
5. Sturgis, C. C., R. Isaacs. *J Clin Invest* 8:663, 1929-30.
6. Means, J. H., J. Lerman, W. B. Castle. *New Eng J Med* 204:243, 1931.
7. Lerman, J., J. H. Means. *Endocrinology*, 16:533, 1932.
8. Heath, C. W., *Amer J Med Sci* 185:365, 1933.
9. Greene, J. A., *Ann Intern Med* 10:622, 1936.
10. McNicol, G. P., *Amer J Med Sci* 241:336, 1961.
11. Tudhope, G. R., G. M. Wilson. *Quart J Med* 29:513, 1960.
12. Holboll, S. A., *Acta Med Scand* 89:526, 1936.
13. Tudhope, G. R., G. M. Wilson. *Lancet* 1:703, 1962.
14. Doniach, D., I. M. Roitt, K. B. Taylor. *Brit Med J* 1:1374, 1963.
15. Schwartz, M. *Lancet* 2:61, 1958.

16-31 May be secured from the Grand Rounds Editor.

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1. Schleif, R.H.: J.A.P.H.A., 46:179,1957 *U.S. Pat. No. 3,062,714

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Book Reviews

We are as liable to be corrupted by books, as by companions.—Fielding

ATLAS OF GENERAL SURGERY — Joseph R. Wilder, Second Edition, C. V. Mosby Company, St. Louis.

Any atlas, by the nature of its intent for the briefest and most basic teaching, presents considerable difficulty for any reviewer, who may and most likely has his own concepts which are at some variance with those presented by the author of such a brief work. Perhaps a surgical atlas would never be totally satisfying to an individual reviewer unless it presented many of the various approaches for solving technical surgical problems. If this were undertaken, it would then hardly fulfill the purpose of an atlas.

This particular atlas might well serve its function in a library of hospitals, where interns and residents could examine it, along with other similar works, to obtain some basic fundamentals of technique.

The introductory comments are succinct and appropriately brief for an atlas. Certain emergency procedures are outlined at the beginning, and these are then followed by a catalog of various general procedures most commonly dealt with in a general hospital. Finally, there is a brief section on certain plastic repairs of tendons and peripheral nerves. The drawings are of good size with reasonably adequate detail.

Under the early section of venous cutdown descriptions, it might have been more appropriate to dwell less on the use of the saphenous vein at the ankle as an avenue of intravenous administration, since none of the shortcomings were outlined, and to have devoted some space to the avenues of central venous pressure and rapid infusion, such as the external jugular, the cephalic, or the sub-clavian vein.

The description of a thyroidectomy appears somewhat incomplete in the method of preserving the blood supply to the parathyroids and the method of identification of the recurrent laryngeal nerve. The author apparently prefers the method of parotidectomy utilizing distal pick-up of the VII nerve branches. Many trained in that method have changed to the method of proximal dissection.

The drawings, or the exposition of Cooper's ligament in the hernia repair, do not appear adequately clear, particularly regarding the repair of femoral hernia.

In the section on biliary surgery, one drawing indicates the direction of the knife blade toward the vital structures of the porta. This, however, is perhaps a very minor criticism. For the section on common bile-

duct injury, the methods of its occurrence are quite timely and useful for the student.

The Roux-Y common duct anastomosis employs a direct end-to-end rather than common duct to buttonhole adjacent to the end of the closed jejunum, so that each side of the common duct risks the hazard of the three-directional closure.

The method of perforated peptic ulcer closure involves plication with no note whatever of the standard Graham closure. This would lead the uninitiated into considerable difficulty in attempting to invert or invaginate the frequently wide zones of induration.

Finally, the operations described for gastric cancer and colonic cancer appear to be somewhat deficient or too brief in their emphasis on proper node dissection for malignancies.

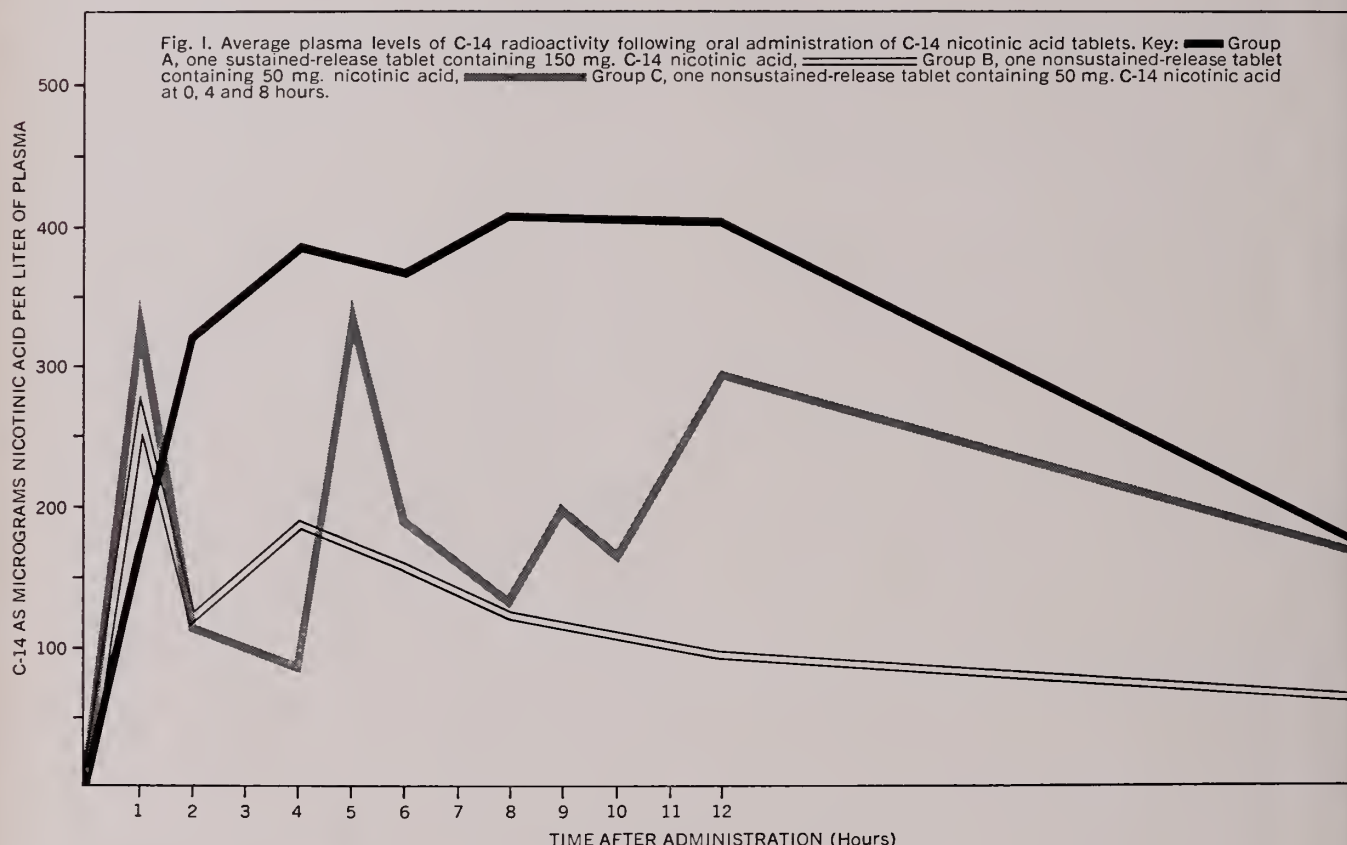
J. H. Strickler, M.D.
Minneapolis, Minnesota

MODERN TREATMENT — Treatment of Neuromuscular Disorders by Frank M. Howard, Jr., M.D.; Treatment of Hypoglycemia by Buris R. Boshell, M.D., Harper and Row, March 1966.

Modern Treatment is a bi-monthly paperback published by Harper and Row through the Hoeber Medical Division. Each volume concerns itself with one or two topics with a guest editor and several contributors. The current issue concerns neuromuscular problems edited by Frank M. Howard and hypoglycemia edited by Buris R. Boshell. Although treatment appears prominently on the cover and in the titles, the contributors have not limited themselves to this narrow approach to medicine. I suspect the publishers have chosen the general title of Modern Treatment since naturally everybody is interested in treatment as the lodestone in medicine attracting all physicians. One need not apologize for considering all aspects of a medical problem under "Treatment", since obviously pathophysiology, diagnosis, and the like, are fundamental to treatment. These two topics are somewhat widely disparate, appealing to different sections of the medical profession. However, one can recommend this volume to all physicians who see general medical problems. Hypoglycemia appears in many guises, including psychoneurosis and psychosis. Myasthenia gravis, admittedly not a common disease, may be primarily seen by any practitioner.

Reuben Berman, M.D.
Minneapolis, Minnesota

Sustained circulatory, respiratory and cerebral stimulation for the



(fewer absent doses by
absent-minded patients)

Human volunteer subjects were administered Geroniazol TT tablets with the nicotinic acid component made radioactive with C-14. Plasma and urine samples were analyzed. (See Figures I and II) The radioactive tracer study substantiated the previous clinical evidence that the release of nicotinic acid from the Geroniazol TT tablet produced a gradual rise in plasma levels to a plateau for a total of 12 hours and more.

Such proven sustained activity makes the management of geriatric patients much easier by minimizing the possibility of neglected doses through absent-

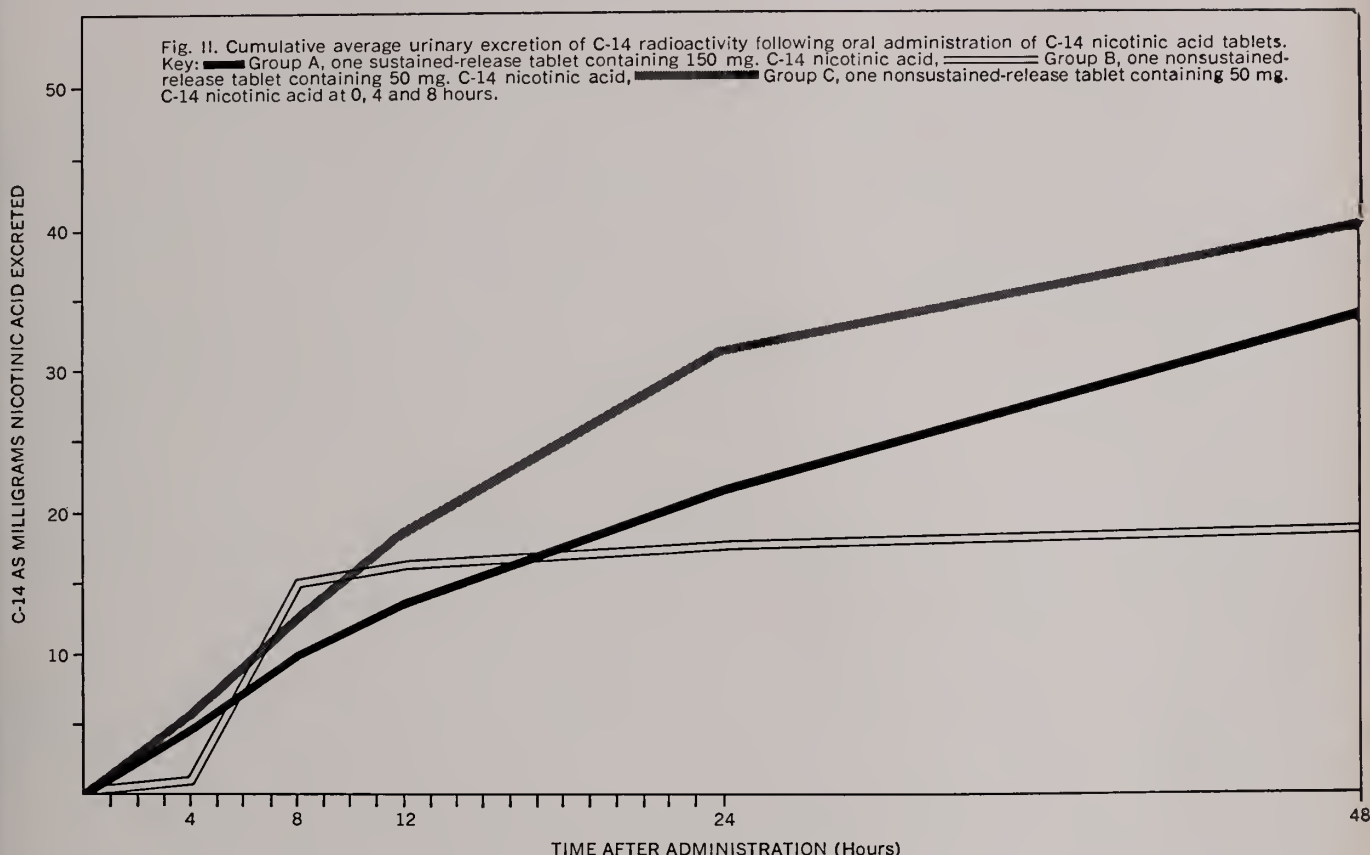
mindedness or senile confusion. Therapy *can* be continuous on a daily dose of only one Geroniazol TT tablet every 12 hours.

The gradual release of nicotinic acid in Geroniazol TT will provide the well-known peripheral vasodilatation needed in patients with deficient circulation and with a minimum amount (if any) of "flushing." Also, cerebrovascular circulation is complemented by pentylentetrazol, long-established as a cerebral and respiratory stimulant.

Geroniazol TT improves the typical, unfortunate, signs of senile confusion. Patients become more alert,

aged and debilitated

Fig. 11. Cumulative average urinary excretion of C-14 radioactivity following oral administration of C-14 nicotinic acid tablets. Key: — Group A, one sustained-release tablet containing 150 mg. C-14 nicotinic acid, — Group B, one nonsustained-release tablet containing 50 mg. C-14 nicotinic acid, — Group C, one nonsustained-release tablet containing 50 mg. C-14 nicotinic acid at 0, 4 and 8 hours.



less confused and moody. Personal care, memory, emotional stability, social attention improve. Fatigue, apathy and irritability are reduced.

A prescription for 100 tablets of Geroniazol TT will permit your patients to enjoy the benefits of time-prolonged nicotinic acid/pentylenetetrazol therapy, at an economical price. Dosage is only one tablet every 12 hours.

Contraindications: There are no known contraindications.

Precautions: Exercise caution when treating patients with a low convulsive threshold.

Side Effects: Side effects are rarely encountered, however due to the vasodilatation effect of nicotinic acid, transitory mild nausea, flushing, tingling and pruritus are possible.

Dosage: One tablet every 12 hours.

Supplied: Prescribe bottles of 100 tablets, to take advantage of recent price reduction.

References: 1. Report by Nuclear Science & Engineering Corp., Pittsburgh, Pa., in files of Philips Roxane Laboratories. 2. Connolly, R.: W. Virginia Med. J. 56:263 (Aug.) 1960. 3. Curran, T. R., and Phelps, D. K.: Am. Pract. & Digest Treat. 11:617 (July) 1960.



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when bursitis hits a 280-lb. tackle, hit back with Butazolidin alka



Indications: Osteoarthritis, rheumatoid arthritis, rheumatoid spondylitis, psoriatic arthritis, acute gout, painful shoulder (peritendinitis, capsulitis, bursitis and acute arthritis of that joint), acute superficial thrombophlebitis.

Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently. Large doses of Butazolidin alka are contraindicated in glaucoma.

Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Pyrazole compounds may potentiate the pharmacologic action of sulfonyleurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage occur. Make regular blood counts. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The most common are nausea, edema and drug rash. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ul-

For 280-lb. tackles — or 108-lb. housewives — Butazolidin alka can hasten recovery from the agonizing pain of shoulder bursitis.

It's not for every patient. Check carefully the Contraindications, Warning and Precautions shown below.

And adverse reactions may occur. The most common are nausea, edema and rash. Rarely, agranulocytosis has been reported. All adverse reactions are listed below, too.

Play-for-pay or workaday patients — when they come up with shoulder bursitis and your clinical judgment indicates Butazolidin alka — go with it.

And watch the comeback.



cer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately before or after meals or with milk to minimize gastric upset. Mild drug rashes frequently subside with reduction of dosage. However, rash accompanied by fever or other systemic reactions usually requires withholding medication. Purpuric rash has also been reported. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, or a generalized allergic reaction similar to serum sickness may occur and require permanent withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

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Dosage in painful shoulder: Initial: 3 to 6 capsules daily in 3 or 4 equal doses. Trial period: 1 week. Maintenance dosage should not exceed 4 capsules daily; response is often achieved with 1 or 2 capsules daily.

For complete details, please see full prescribing information.

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WANTED: General practitioner, to join two G.P.'s well established in north central Minnesota community, 2200 pop., 65 miles from Twin Cities. Excellent office space with lab and X-ray, just opened new hospital, all facilities. Assistantship or partnership. Considerable surgery and obstetrics. Hunting, fishing, golf club. Great opening for interested G.P. WRITE MINNESOTA MEDICINE—381; 375 Jackson, St. Paul, 55101.

GENERAL PRACTITIONER wanted to join well-established practitioner. New clinic building—90 miles east of St. Paul—city of 14,000. Early partnership with full hospital facilities. Ideal location. L. W. Picotte, M.D.; Chippewa Falls, Wisconsin.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X-ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE—289; 375 Jackson, St. Paul, 55101.

GENERAL PRACTITIONERS AND INTERNISTS to join eight-man group in fascinating San Francisco. Locum tenens also available. Will meet reasonable salary request. A. J. Franzi, M.D., 3620 Army St., San Francisco, Calif. 94110.

WANTED GENERAL PRACTITIONER, General Surgeon, Obstetrician for active group clinic in Minneapolis suburb. Now six man group including full time surgeon and obstetrician. New clinic facilities and two new hospitals near by. Salary open. Partnership offered after short trial period. Coon Rapids Clinic, 9920 Zilla Street, N.W., Coon Rapids, Minn. 55433.

WANTED: GENERAL SURGEON to fill vacancy with well established eight man group. Beautiful award winning clinic just blocks from new 120 bed hospital. Picturesque community of 15,000 located on the Mississippi River with good recreational facilities, schools and churches. An excellent opportunity in a growing environment. Salary one year, then partnership. Write: Harry Williams, M.D., Medical Block Clinic, Red Wing, Minnesota, or call 507, 388-4751.

GENERAL PRACTITIONER desires position with group or partnership in town of 3000 population or more, preferably within 100 miles radius of Twin Cities. Currently in solo practice including surgery and OB at same location for 12 years. Write: MINNESOTA MEDICINE—383, 375 Jackson, St. Paul, 55101.

WANTED: Young, energetic General Practitioner to join one man clinic. Salary open. Contact: Maurice Meller, M.D., Brainerd Clinic, Brainerd, Minnesota.

INTERNIST, PEDIATRICIAN and OB-gynecologist wanted to join two general surgeons in a rapidly growing practice. Attractive town of 3,000 on large lake 30 miles west of Twin Cities. New 55-bed JCAH hospital with plans for major expansion. Five other physicians in town. No OB-GYN, internist or pediatrician in area. Medical community serves in an area with population of 20,000 to 25,000. Planning to expand into partnership multi-specialty clinic. Call or write: Savaryn Clinic, Waconia, Minnesota 55387. Telephone: 442-2137.

WANTED: Locum Tenens for general practice for February 1968. Salary open. Contact: Maurice Meller, M.D., Brainerd Clinic, Brainerd, Minnesota.

THREE MAN group in North West Wisconsin Resort, State Conservation and Retirement Area needs two more physicians adequately to serve their practice. Facilities offered are three-room physician suites, X-ray and lab under AMT technician, RN-only nursing personnel. New accredited thirty-two bed hospital and forty-six bed nursing home. Deer and duck hunting, fishing within five minutes of town. Internist most needed; generalists welcomed. Will meet any reasonable salary request. Partnership after one year. Write: MINNESOTA MEDICINE—365; 496 Lowry Medical Arts Building, St. Paul 55102.

PHYSICIAN INTERESTED in internal medicine wanted for Medical Service. Starting salary \$12,873 to \$17,221, depending on qualifications. Liberal fringe benefits. Non-discrimination in employment. Contact Chief of Staff, Veterans Administration Hospital, Des Moines, Iowa 50308.

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WANTED: YOUNG PHYSICIAN for association leading to partnership with four well-established General Practitioners in fast-growing suburb of St. Paul. Excellent clinic facilities in nearly new, partnership owned, well equipped, medical center building. Contact: A. Eugene Muller, M.D., North St. Paul Medical Center, 2579 East 7th Avenue, North St. Paul, Minnesota 55109.

WANTED: PEDIATRICIAN, certified or eligible, to associate with two certified pediatricians in upper mid-west college city of 50,000. Write: MINNESOTA MEDICINE—387, 375 Jackson, St. Paul 55101.

WANTED: ASSOCIATE for young general practitioner. Excellent clinic and hospital facilities. Salary or partnership. Agricultural and resort area, good hunting and fishing. Write: Lewis E. Struthers, M.D., Parker Prairie, Minnesota. Telephone: 218-338-4471 (residence) or 218-338-4371 (clinic).

PHYSICIAN WANTED: G.P. with additional surgical and O.B. experience — desired to associate with two G.P.'s with similar experience in large, well established practice in Central Minnesota. Hospital accredited, 300 bed, open staff, complete services. Salary leading to partnership. Adequate housing in area. Send background information, professional and personal to: MINNESOTA MEDICINE, Box 283, 496 Lowry Medical Arts Bldg., St. Paul, 55102.

MORGAN, MINNESOTA, Wants a General Practitioner. Opportunity to take over a well established practice. Physician recently retired after practicing here for 33 years. Progressive community in the best rural area of Southern Minnesota. New medical clinic building just completed. Call or write M. L. Kuhn, Morgan, Minnesota. Tel. Morgan #73 or #99.

SAN FRANCISCO AREA: G.P.'s and/or Internists to associate with group in fascinating Bay Area; Salary open. Partnership and locum tenens available. A. J. Franz, M.D., 3620 Army St., San Francisco, Calif. 94110.

GENERAL PRACTITIONER OR INTERNIST needed in six man group in Northeastern Minnesota. 38 bed accredited hospital next door to modern clinic, rotating call schedule, over 4 wks. vacation per year, study and sick leave, group paid disability and retirement plans, and full partnership in 6 months. Starting guarantee \$18,000 to \$22,000 with increases to \$26,000 to \$28,000 over 4 years. Ideal opportunity for man desiring association with active group in small community offering good income plus ample time off. Contact Harold B. Leppink, M.D., Community Clinic, Two Harbors, Minnesota. Phone Area 218 834-2171.

WANTED: INTERNIST to enlarge busy internal medicine department in highly successful nine man specialty group. All are board certified. Well equipped lab and x-ray—new 120 bed hospital. Pleasant community of 15,000+ on Mississippi River. Good recreational facilities, not far from Twin Cities. Salary one year then partnership. Write George E. Jackish, M.D. —Interstate Clinic, Red Wing, Minnesota or call 507 388-3503.

GENERAL PRACTITIONER WANTED—Ipswich, S. Dak. pop. 1200 is losing one of two doctors. New \$360,000 Hospital opened Oct. 1965. County seat town & only Medical Center in County of 6,000 pop. Desirable office space available. Good school, good hunting & fishing, no riots, potential practice: Excellent. Call collect or write: Earle T. Crissman, Ipswich, S. Dak. phone—day 5111, night—4551.

Bilateral Vestibular Paralysis Syndrome

Complete loss of vestibular function in man was demonstrated clinically by James in 1882. Clinical features include a staggering gait as well as a broad base when walking in the dark or with eyes closed. There is inability to fix the eyes upon an object while moving the head. With the eyes closed there is complete disorientation in water. Coloric or rotation tests for labyrinthine function show no evidence of vertigo, unsteadiness, nausea, nystagmus, or past pointing. In four cases (Chusid and de Gutierrez-Mahoney) the etiology was attributed to an infectious process including scarlet fever, scrub typhus, and syphilis.

Durham, Robert H. — Encyclopedia of Medical Syndromes
Hoeber Medical Division, Harper and Row, New York

Remedies For Boils

For the cure of boils, beef-suet is applied with salt; but if they are attended with pain, it is melted with oil, and no salt is used. Goat-suet is employed in a similar manner.—Pliny.

Tired or Curious

Men marry because they are tired, women because they are curious. Both are disappointed.—Wilde.



Physician's Diary

The insolent civility of a proud man is, if possible, more shocking than his rudeness could be; because he shows you by his manner, that he thinks it mere condescension in him, and that his goodness alone bestows upon you what you have no pretence to claim.—Chesterfield.

Dr. John L. Juergens, consulting physician in internal medicine at the Mayo Clinic, is the new president of the Minnesota Heart Association. Dr. James H. Kelly, St. Cloud, was elected president-elect; Mr. E. William Quirin, Rochester, second vice-president, Dr. John Fee, St. Paul, secretary; and Dr. John L. Olson, St. Paul, treasurer.

* * *

Dr. Charles A. Neumeister has been re-elected president of the Blue Shield of Minnesota, Dr. Harold Mork, Anoka, was elected to the Board of Directors, and Dr. John G. Lohmann, Pipestone, was elected Treasurer.

* * *

Dr. Robert L. Radke of Montevideo and Dr. Elmer Keithahn, Sleepy Eye, have been reelected to active membership in the American Academy of General Practice, and Dr. Donald E. Wohlrabe, Springfield, and Dr. David R. Holten, Edina, have been elected to active membership in the same Academy.

* * *

Dr. Edward A. Banner, member of the Section of Obstetrics and Gynecology of the Mayo Clinic, was chosen president-elect of the Continental Gynecologic Society at its annual meeting in May.

* * *

Dr. John C. Duffy has been named chief consulting psychiatrist for the Minnesota Residential Treatment Center in Circle Pines.

* * *

Dr. Michael M. Paparella has been appointed head of the Department of Otolaryngology at the University of Minnesota College of Medical Sciences and Dr. Robert Mulhausen, assistant chief of medicine at Veterans Hospital, Minneapolis, has been named assistant dean of the University of Minnesota College of Medical Sciences.

* * *

Dr. John A. Docherty, Medical Director of Anoka State Hospital, accepted an appointment as a full-time member of the Medical Staff at Hennepin County General Hospital and Hennepin County Mental Health Center. This became effective August

16. Dr. Guido H. Schynoll has been appointed Acting Medical Director of the Anoka State Hospital.

* * *

New Location: Dr. David J. Lamusga is now associated with the Mora Clinic in Mora. . . . Dr. A. E. Carlson, Warren physician, has moved to Fargo where he will be senior physician at the Veterans Hospital. . . . Dr. George W. Ibrahim has joined the Lenont-Peterson Clinic in Virginia. . . . Dr. E. P. Bryant has resigned his position on the medical staff of the Faribault State School and will resume his practice on a full-time basis in Ellendale. . . . Dr. Robert Pierce will practice medicine on a part-time basis in Mountain Lake and Heron Lake dividing his time between the two communities. . . . Dr. Mustafa Vidinli has left Roseau for Aurora, Illinois, to do some research work at Northwestern University. . . . Dr. Gerardo A. Crichigno has joined the medical staff at Hastings State Hospital. . . . Dr. O. B. Fesenmaier, Brown County coroner and New Ulm physician, has taken a one-year leave of absence from his medical practice to do graduate work in Los Angeles. . . . Dr. Roger A. Dreyling has joined the Paynesville Community Hospital staff. . . . Dr. W. F. Schamber has left Parkers Prairie to assume duties as staff doctor at the Veterans Hospital in St. Cloud. . . . Dr. Roland Larter has joined the Karlstad Memorial Hospital. . . . Dr. A. H. Field, Burnsville, has accepted a position with the University of Arizona. . . . Dr. Lewis E. Struthers is the new doctor for Parkers Prairie. . . . Dr. Norbert O'Keefe has joined the Quain and Ramstead Clinic in Bismarck. . . . Dr. David Sweet has become associated with Doctors Thayer, Wandke and Kraemer in Fairmont. . . . Dr. Kenneth L. Buresh has joined the Owatonna Clinic. . . . Dr. Gerald Cotton has left Fosston to take up a fellowship in Internal Medicine at the Mayo Graduate School of Medicine. . . . Dr. James Garber has joined the Olmsted Medical Group in Rochester. . . . Dr. A. L. Ourada has left Ceylon to accept a four-year residency training program at St. Paul Ramsey Hospital in St. Paul. . . . Dr. James Terrian has joined the Klefstad Clinic in Greenbush. . . . Dr. Donald Mattson has joined the medical staff of the Lakeland Medical Center in Willmar.

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Plan to attend this year's AMA Clinical Convention in Houston, Texas. Eighteen scientific sessions, four postgraduate courses, breakfast roundtable discussions, color television, and scientific and industrial exhibits will bring you up to date on the latest medical advances. Attend lectures by, and discussions with, our nation's outstanding medical authorities.

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SCIENTIFIC SESSIONS: Cardiovascular Disease; Cardiovascular Surgery; New Cares; Ophthalmology; Geriatrics; Arthritis; Gastroenterology; Cancer; Antibiotics; Endocrinology; General Surgery; Dermatology; Aerospace Medicine; Obstetrics and Gynecology; Psychiatry; Pediatrics; Genitourinary Diseases; and Otolaryngology.

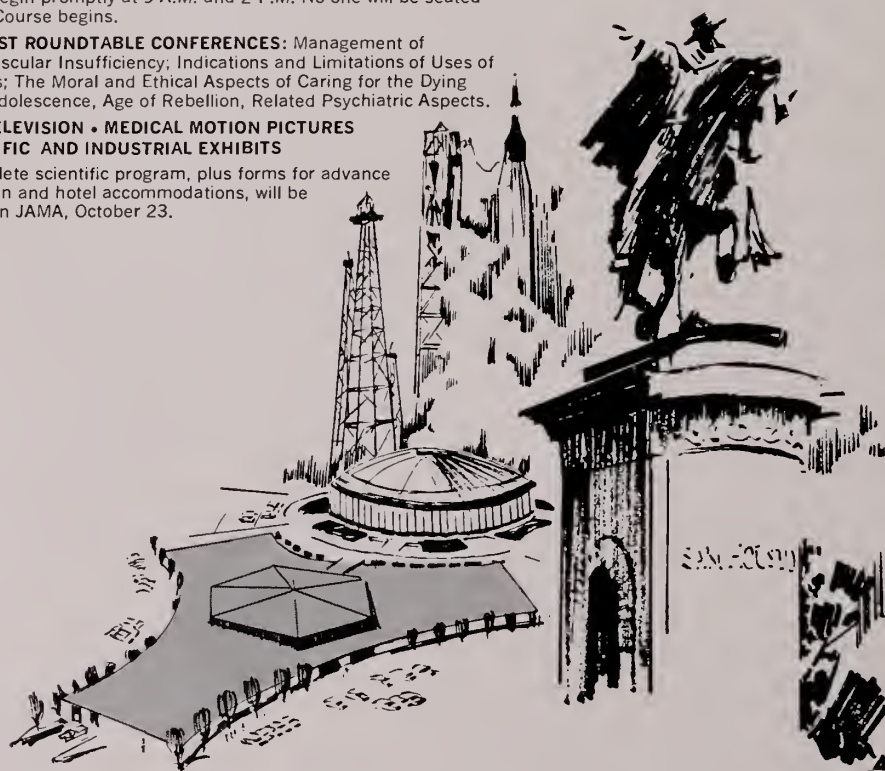
POSTGRADUATE COURSES: Fluid and Electrolyte Balance; Oncology; Cardiovascular Disease; and Obstetrics and Gynecology. Register for these Courses on arrival in Houston at the PG Course Registration booth adjacent to the General Registration area. There is no charge for the Courses, but registration is limited to 200 per Course. The Courses begin promptly at 9 A.M. and 2 P.M. No one will be seated after the Course begins.

BREAKFAST ROUNDTABLE CONFERENCES: Management of Cerebrovascular Insufficiency; Indications and Limitations of Uses of Antibiotics; The Moral and Ethical Aspects of Caring for the Dying Patient; Adolescence, Age of Rebellion, Related Psychiatric Aspects.

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The complete scientific program, plus forms for advance registration and hotel accommodations, will be featured in JAMA, October 23.





Meetings and Announcements

Our knowledge is the amassed thought and experience of innumerable minds
—Emerson

OCTOBER

Hennepin County Academy of General Practice, October 2, Membership Meeting, Pick-Nicollet Hotel, 6:00 P.M. Social Hour; 6:45 Dinner, 7:45 Business meeting.

Hennepin County Medical Society, Pick-Nicollet Hotel, October 2, 6:00 P.M. Social Hour; 6:45 Dinner, 7:45 Business meeting, 8:15 Sectional meetings.

Southwestern Minnesota Medical Society, October 2, Ehlers Supper Club, 7:00 P.M.

Lyon-Lincoln County Medical Society, Clinical Lectures, Chalet Club, Marshall, October 3, 10, 17, 24, 6:30 P.M.

Scott-Carver County Medical Society, October 3, Wagner Supper Club, Jordan, Minnesota, 7:30 P.M.

St. Louis County Medical Society, Executive Committee, St. Luke's Hospital, 6:00 P.M., Regular Meeting, St. Luke's Hospital, 8:00 P.M., October 12.

Hennepin County Academy of General Practice Membership Meeting, Minneapolis Athletic Club, October 16, 6:00 P.M. Social Hour; 7:00 P.M. Dinner, 8:00 P.M. Program.

Minnesota Society of Internal Medicine, October 16, Rochester, Minnesota.

Blue Earth Valley Medical Society, October 18, Interlaken Golf Club, Fairmont, Minnesota, 7:00 P.M.

McLeod County Medical Society, October 19.

Twin City Urologic Society, October 20, Town and Country Club, St. Paul, 6:00 P.M.

Ramsey County Medical Society, Clinical Meeting (Subject to change), October 30, St. Paul-Ramsey Hospital, 8:00 P.M.

Lyon-Lincoln County Medical Society, Annual Meeting, Chalet Club, Marshall, Minnesota, 6:30 P.M., October 31.

NOVEMBER

Minnesota Academy of Ophthalmology and Otolaryngology, No date set as yet.

Minnesota Psychiatric Society, Fall meeting, No date set as yet.

Zumbro Valley Medical Society, Regular Meeting, Plummer Hall, 8:00 P.M., November 1.

Southwestern Minnesota Medical Society, November 6, Ehlers Supper Club, 7:00 P.M.

Scott-Carver County Medical Society, November 7, Wagner Supper Club, Jordan, Minnesota, 7:30 P.M.

St. Louis County Medical Society, Executive Committee, St. Mary's Hospital, 6:00 P.M., Regular Meeting, St. Mary's Hospital, 8:00 P.M., November 9.

Blue Earth Valley Medical Society, November 15, Interlaken Golf Club, Fairmont, Minnesota, 7:00 P.M.

McLeod County Medical Society, November 16.

Twin City Urologic Society, November 17, Town and Country Club, St. Paul, 6:00 P.M.

Hennepin County Academy of General Practice Annual Invitational Banquet, Radisson Hotel, Minneapolis, 6:00 P.M. Social Hour, 7:00 P.M. Dinner, 8:00 P.M. Program, November 20.

Ramsey County Medical Society Regular Meeting, 1500 Lowry Medical Arts Building, St. Paul, 8:00 P.M., November 27.

Range Medical Society Regular Meeting, Hibbing, Minnesota, November 28, 7:00 P.M.

DECEMBER

Minnesota OB-GYN Society, St. Paul-Ramsey Hospital, 9:00 A.M., December 2.

Southwestern Minnesota Medical Society, December 4, Ehlers Supper Club, 7:00 P.M.

Scott-Carver County Medical Society, December 5, Wagner Supper Club, Jordan, Minnesota, 7:30 P.M.

St. Louis County Medical Society Executive Committee, St. Luke's Hospital, 6:00 P.M., December 14. Annual Banquet, Kitchi Gammi Club, 7:30 P.M., December 16.

McLeod County Medical Society, December 21.

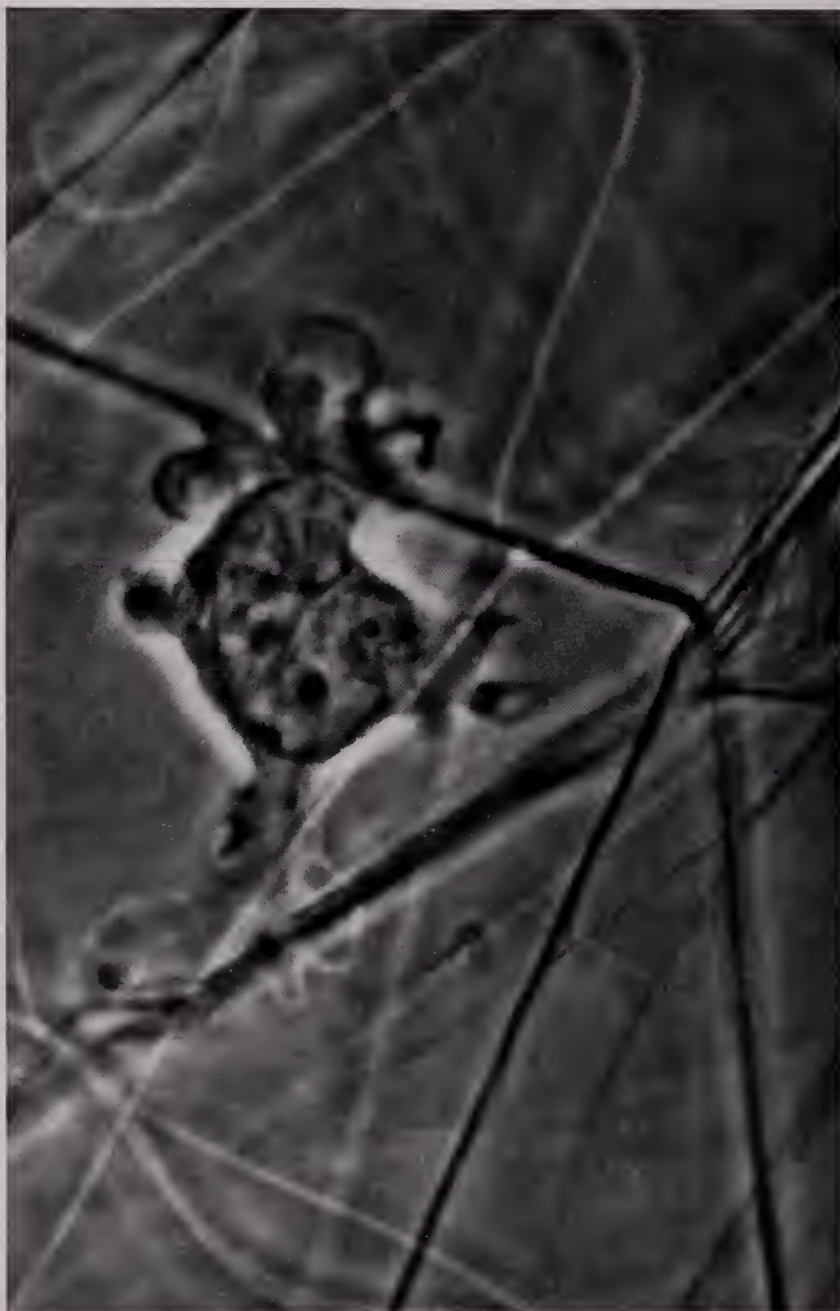
Minnesota Academy of Ophthalmology and Otolaryngology. No date set as yet.

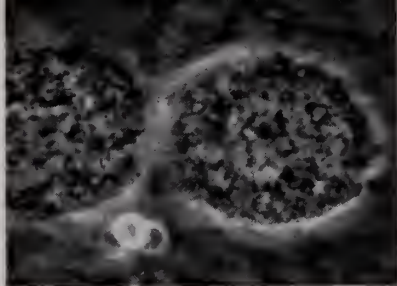
INFLAMMATION: A cellular fight for life

A SYNTEX REPORT based on recently developed hypotheses about topical corticosteroids, including the cellular theories of inflammation by Thomas F. Dougherty, Ph.D., University of Utah.

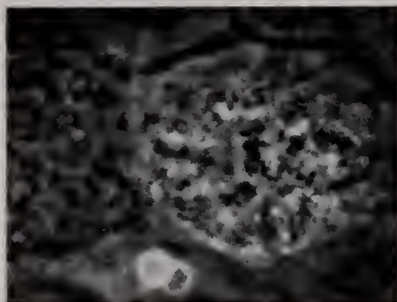
You are looking at a fibroblast fighting for life. This cell—one of the most common found in connective tissue—has literally been poisoned by cytotoxins released from other cells that have ruptured. Soon, if the abnormal activity of this fibroblast does not cease, it, too, will rupture and die—one more casualty in the inflammatory wave of destruction precipitated by injury.

Until a short time ago no one had ever witnessed such a scene at the cellular level. Now, through advanced cinemicrographic techniques, it is possible to view and photograph the inflammatory process as produced experimentally in living animal tissue. This method permits new insight into the mechanism of inflammation and the role of corticosteroids in therapeutic management. Equally important, these techniques shed new light on factors that may make one corticosteroid more effective than another—factors that can be correlated with other chemical, biologic, and clinical parameters.





Phase-contrast microscopy showing mast cell before injury.



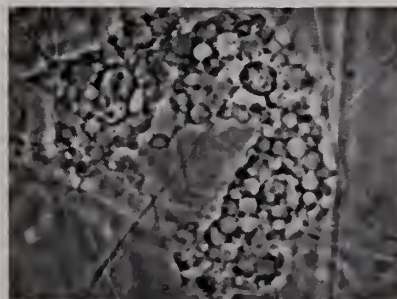
Mast cell (after injury) has broken up and released cytotoxins.

How corticosteroids change the picture

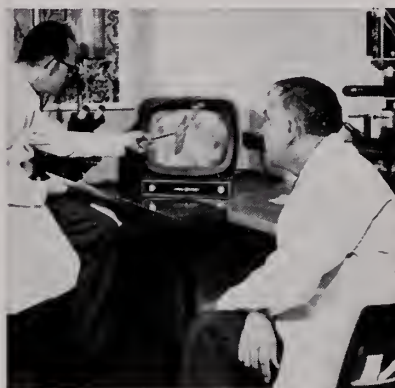
Corticosteroids appear to virtually stop the abnormal cellular activity that constitutes the inflammatory reaction. This permits the body's natural resources to clear up the inflamed area and repair the damaged tissue. This interpretation is supported by the fact that when the injurious gelatin solution is injected simultaneously with a corticosteroid — Synalar (fluocinolone acetonide) — the inflammatory pattern simply does not develop.



Fibroblast in high state of activity, much distorted.



Mast cells showing effects of corticosteroid action: cells are normal in size, shape and activity.



In summarizing his study Doctor Dougherty states: "...we also feel this work may explain why one corticosteroid helps a patient more rapidly and effectively than another. If it does, it is because one corticosteroid is the fastest, most effective inhibitor of the series of inflammatory events at the tissue level."

**A New View of Corticosteroid Action in Inflammatory Dermatoses, a film based on this study, is now available from your Syntex representative.*

Visual evidence of how corticosteroids influence the inflammatory reaction

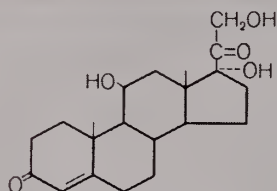
Working with phase-contrast cine-micrography on living animal tissue, Doctors Thomas F. Dougherty and David Berliner of the University of Utah College of Medicine have actually filmed cellular events that occur during the inflammatory reaction. This remarkable study* and additional work by these investigators, as well as by others, have established a new theoretical biologic basis for the antiinflammatory effect of the corticosteroids. (It must be noted that other theories, such as the lysosome or so-called "suicide bag" theory, have been postulated, although it is quite likely that there are more similarities than differences among the various theoretical models.)

The inflammatory wave of destruction

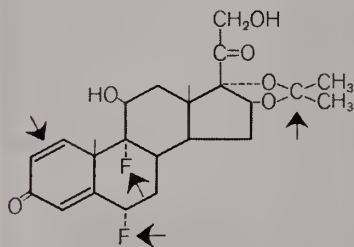
In this investigation an injurious injection of gelatin is used to set off an inflammatory reaction in living mouse tissue. What follows is a wave of destructive cellular activity that comprises the inflammatory response to injury. Mast cells (which contain heparin, serotonin and histamine) take up water, swell and rupture, releasing their contents, which are toxic outside the mast cell wall. These toxins, in turn, cause disintegration of other cells (such as fibroblasts) and the release of additional toxic material. Capillaries, too, take up water and leak unformed blood elements, causing edema. And polymorphonuclears, lymphocytes and perithelial cells invade the inflamed site. As a result of all these changes, the cellular environment reaches a state of turmoil.

How advances in chemical design have achieved greater steroid potency

The chemical modification of corticosteroid molecules from the advent of hydrocortisone to the development of Synalar (fluocinolone acetonide) is a prime example of how biochemists can "design" to increase therapeutic activity and minimize undesirable side actions. Below, for example, we see the important changes that were made in reference to the hydrocortisone molecule to produce fluocinolone acetonide, one of the most active of all topical corticosteroids. As a result, a 0.01% preparation of Synalar (fluocinolone acetonide) has been reported to do the work of a 1% hydrocortisone product containing 100 times more corticosteroid. And it can often do it more effectively.



Hydrocortisone

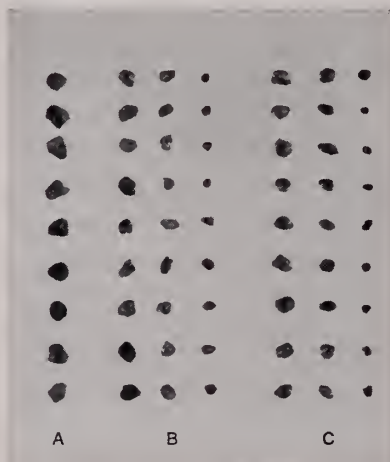


Fluocinolone Acetonide (Synalar)

- ☐ a double bond between carbons 1 and 2
- ☐ fluorine substitutions at both the 6- α , and the 9- α positions
- ☐ the addition of the acetonide at the 16- α , 17- α positions, thus providing one of the most potent topical corticosteroids available.

How bioassay tests are used to "predict" therapeutic potential

Biologic assays are another tool used by researchers to help establish the relative activity of corticosteroids. To date no single method of assaying corticosteroid activity has emerged as the ideal "yardstick" for predicting therapeutic potential. Taken together, however, these methods have proved useful. When such tests are run on various corticosteroids, a definite order of corticosteroid activity becomes evident. Compounds with the highest order of activity may be expected to merit clinical trial to establish their high therapeutic potential. When assayed by these methods, fluocinolone acetonide (Synalar) emerges as one of the most active topical corticosteroids, milligram for milligram, available for clinical application today.



THE THYMUS INVOLUTION ASSAY¹⁻⁴ is run on adrenalectomized rats. The sizes of the glands are measured, and the degree of involution caused by the steroid is determined as an indication of its potency. In the above photo, the comparative involution of thymus glands achieved with hydrocortisone and Synalar (fluocinolone acetonide) is shown. Untreated controls (A) show normal size. Group B— injected with 1, 2 and 4 mg. of hydrocortisone— show progressively smaller thymuses as does Group C— injected with fluocinolone acetonide— but with only 1/500th the dose of hydrocortisone.



THE ANTIGRANULOMA ASSAY¹⁻⁴ also utilizes adrenalectomized rats. Granulomas are induced by subcutaneous implantation of cotton pellets on either side of the thorax. The degree of granuloma inhibition achieved by a steroid reflects its potency. The above photo shows the inhibition of granuloma formation achieved with hydrocortisone and Synalar (fluocinolone acetonide). Untreated controls (A) show large, red granulomas adhering to the pellets. Group B, receiving hydrocortisone and Group C, receiving fluocinolone acetonide, show little, if any, granuloma formation. Fluocinolone acetonide produced the same effect as hydrocortisone with only 1/500th the dose. This assay, as well as the thymus involution assay, measures systemic rather than topical corticosteroid activity. Nevertheless, results by these methods correlate well with other assays and with the milligram potencies of topical steroids in current clinical use.

Worldwide clinical experience confirms the predictable therapeutic potential of Synalar

It is particularly gratifying that the promise of the advanced chemical design and high order of bioassay activity of Synalar (fluocinolone acetonide) has been confirmed by widespread therapeutic application. Indeed, the impressive clinical response rate of Synalar has been documented in no fewer than 232 papers from 22 countries.

PRESCRIBING INFORMATION

For initiation of therapy: Cream 0.025%, 5 and 15 Gm. tubes, 425 Gm. jars; *for emollient effect:* Ointment 0.025%, 15 Gm. tubes; *for maintenance therapy:* Cream 0.01%, 15 and 45 Gm. tubes, 120 Gm. jars; *for intertriginous or hairy sites:* Solution 0.01%, 20 cc. and 60 cc. plastic squeeze bottles; *for infected inflammatory dermatoses:* Neo-Synalar® Cream (0.025% fluocinolone acetonide, neomycin sulfate, equivalent to 0.35% neomycin base), 5 and 15 Gm. tubes.

CONTRAINDICATIONS: Tuberculous, fungal, and most viral lesions of the skin, (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components. **PRECAUTIONS:** Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for pro-

Representative Clinical Results with Synalar*

Efficacy Documented in over 4,000 Patients

Condition	Number of Publications	Number of Patients	Significant Improvement†
Contact Dermatitis	27	750	713
Eczematous Dermatitis	21	472	409
Seborrheic Dermatitis	18	442	426
Atopic Dermatitis	24	460	426
Psoriasis	36	1,699	1,510
Neurodermatitis	18	351	324
Total	144	4,174	3,808

*Complete bibliography on request.

†Expressed by the authors as excellent, very good, good, complete remission of inflammation, etc.

longed periods of time. Prolonged use of any antibiotic may result in overgrowth of nonsusceptible organisms; if this occurs, appropriate therapy should be instituted. When severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. **SIDE EFFECTS:** Side effects are not ordinarily encountered with topically applied corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. The neomycin in Neo-Synalar Cream rarely produces allergic reactions.

REFERENCES: 1. Lerner, L. J., Bianchi, A., Turkheimer, A. R., Singer, F. M., and Borman, A.: Anti-inflammatory steroids: potency, duration and modification of activities. *Ann NY Acad Sci* 116:1071 (Aug. 27) 1964. 2. Idem: Comparison of anti-granuloma, thymolytic and glucocorticoid activities of anti-inflammatory steroids. *Proc Soc Exp Biol Med* 116:385 (June) 1964. 3. Ringler, A.: Activities of adrenocorticosteroids in experimental animals and man, in Dorfman, R. I.: *Methods of hormone research*, New York, Academic Press, 1964, vol. III, pp. 234-280. 4. Gubersky, V. R.: To be published.

fluocinolone acetonide — an original steroid from
SYNTEX
LABORATORIES INC., PALO ALTO, CALIF.

For inflammatory
dermatoses...
by any measure
a topical corticosteroid
of choice

Synalar® (fluocinolone acetonide)

Milligram for milligram
one of the most active topical
corticosteroids available

Rapid and predictable
in antiinflammatory and
antipruritic activity

Results often comparable to
those of systemic corticosteroids
with fewer hazards



I told you it was void without a signature

Unless each claim has a
valid signature the claim is void
and must be returned to you.

BLUE SHIELD
OF MINNESOTA



Law and Medicine

Code of Interprofessional Relations

Minnesota State Bar Association
Minnesota State Medical Association

The Medical Advisory Committee of the Minnesota State Medical Association wishes to call your attention to the Code for Interprofessional Relations of the Minnesota State Medical Association and the Minnesota State Bar Association which was adopted by both Associations in 1960. It is published in the October issue of MINNESOTA MEDICINE in response to many requests received by the committee recently for copies. It has also been published in a recent issue of the BENCH AND BAR OF MINNESOTA, and the committee suggests that you review the entire code with a view to its pertinence and effectiveness. If you have any comments or proposals for amendments please let the committee know.

Donald C. MacKinnon, Chairman

Preamble

Acknowledging that a substantial part of the practice of law and medicine is concerned with the problems of persons who are in need of the combined services of an attorney-at-law (hereinafter called lawyer) and a doctor of medicine (hereinafter called physician), and that the public interest and individual problems in these circumstances are best served by the cooperative efforts of all concerned, we, the members of the Minnesota State Bar Association and the Minnesota State Medical Association, do hereby adopt the following interprofessional code as the standard for proper, ethical conduct for lawyers and physicians.

Interprofessional Relations

Physicians and lawyers, as members of learned professions, have much in common. The state licenses the members of each profession to administer to the needs of and to carry out social responsibility to the public. Each is dedicated to the principle of free choice—freedom of choice in the selection of a physician to safeguard the health of the individual, and freedom of choice in the selection of a lawyer to safeguard an individual's freedoms and rights as a citizen. Each is bound by a code of ethics dedicated to the most worthy objectives inherent in the trust placed in each profession by the community.

The physician has responsibility for the care of his patient, not only in health but also in

disease and injury. He is the adviser and confidant of his patient in matters of health. He must administer to the needs of his patient to the best of his ability and in accordance with the high precepts of the Hippocratic Oath.

The lawyer represents his client as advocate in legal proceedings and as counsellor in business and personal affairs. He is the adviser and confidant of his client in legal matters. He performs his duties as an officer of the court, sworn to support and defend the Constitution of the United States and of the state or states in which he is admitted to practice with high standards of conscience and morality.

The members of each profession are pledged to maintain the confidence and to preserve inviolate the secrets of their patients or clients, as the case may be.

Each profession is obligated by its own stature to respect and honor the calling of the other. Neither the fact nor the appearance of incompetence, corruption, dishonesty or unethical conduct on the part of individual members of either profession can be tolerated. It, therefore, follows that each profession must vigorously support within its own ranks, as well as within the ranks of the other, those ethical concepts which each has found necessary in the public good. But when doing so, the members of each profession must keep in mind that the members of the other profession have been found competent to be such by ap-

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propriate authority, that there are differences in the capacities and characteristics of the practitioners of the other profession, and that while law and medicine may each be termed a science, each is an inexact science and such inexactness is and always will be accentuated by the human limitations of its practitioners.

This interprofessional code constitutes recognition that with the great development in the science and art of both medicine and law, physicians and lawyers are drawn into more and more associations, as the law calls with increasing frequency upon medicine for its scientific knowledge and its evaluation of facts so that the rights of individuals may be appropriately determined before various tribunals.

I. Medico-Legal Aspects Before Trial

The physician becomes involved in the legal process either because he has been engaged for the purpose of diagnosis, care or treatment of some patient whose legal rights are being litigated or because he has been engaged for the purpose of litigation rather than for diagnosis, care or treatment. If he is a physician engaged for the purpose of diagnosis, care or treatment, he will be referred to herein as the attending physician, whether he was the physician who treated the patient during the entire course of his illness or injury or the physician called as a specialist with respect to certain aspects of diagnosis, care or treatment of the patient. If he is a physician engaged for the purpose of litigation, he will be referred to herein as the examining physician.

A. Professional Obligation of Physician to Patient in Regards to Litigation

The attending physician has a duty to assist his patient with respect to any litigation involving the conditions which the physician has treated. This duty arises from his general obligation to assist in the administration of justice and his specific responsibility for the welfare of his patient.

Administration of justice is essential to orderly society. An effective system for settlement of claims involving the physical or mental condition of a person is essential to judicial administration. Disposition of such claims either by trial or in anticipation of trial must be

based on facts relating to (1) liability and (2) damages. The attending physician, by virtue of the confidence reposed in him by his patient has unique knowledge of the physical and mental condition of his patient; the care and treatment required; and the degree of permanent loss, if any, to be anticipated. The issue of damages cannot be fairly resolved without these facts.

It is for the physician to determine the actuality or probability of facts pertaining to his patient's condition. It is for the lawyer to determine when, how and under what circumstances such facts are most appropriately to be presented.

B. Medical Conduct Before Trial

The information obtained by the attending physician in the course of his examination and treatment of a patient and any written report thereof are legally privileged, except that in situations involving the Workmen's Compensation Act an attending physician designated by the Commission or whose services are paid for by the employer may be required to testify as to any information acquired by him in the course of treatment or examination. The information obtained by an examining physician and any written report thereof are not privileged. Nevertheless, an examining physician should not reveal such information or the contents of such report to anyone other than the person employing him without first obtaining the written consent of such person.

Neither the attending physician nor the examining physician should express any opinion to the patient as to the settlement value of any claim for personal injury.

The examining physician, acting for a party adverse to the person he is examining, should, where taking a medical history, attempt to elicit only such facts as are pertinent to his examination; he should not attempt to obtain statements which might constitute admissions with reference to any accident out of which the litigation arises. Such an examining physician should not solicit the findings or the opinions of or consult with the attending physician, nor should he suggest to the person being examined any treatment, comment to such a person on any treatment already received, or divulge to such person any of his medical findings or opinions.

It is not desirable for a lawyer to be present when his client is being examined by an examining physician whether the physician is employed on behalf of his client or on behalf of an adverse party, but there is no reason why the lawyer should not discuss with such physician, either before or after examination, any aspect of the examination that may be pertinent.

C. Legal Conduct Before Trial

A frank discussion of the issues and opinions between the physician on the one hand and the lawyer on the other hand prior to trial is to be encouraged. The lawyer may properly point out the legal foundation for medical evidence and the reasons for it. This does not, however, mean that the physician's testimony must be in accord with these views, for a lawyer by his conscience and his ethics is prohibited from attempting to color or distort the professional opinion of a physician to be called as a medical witness in the trial of a case. Both the lawyer and the physician must share the responsibility for improperly presented or fraudulent medical testimony. Such testimony is unworthy of both professions.

D. Medical Reports

The physician should always stand ready to furnish written reports to lawyers. This statement applies not only to examining physicians but also to attending physicians. The lawyer when requesting a written report from a physician concerning the condition of a patient should make his request in writing and should direct the physician's attention to the particular condition which interests the lawyer.

The lawyer should not expect the attending physician to furnish a report unless the physician has first received a written authorization from the patient permitting the physician to furnish such a report, or the lawyer's letter to the physician contains a signed acknowledgment by the patient of the lawyer's authority to act in his behalf.

A request for a written report should ask for history, diagnosis, treatment, prognosis and medical fees up to the date of the report.

The physician has an obligation to keep adequate records which may be used to supply to

a patient's lawyer all information regarding the patient-client's medical history, and to retain control of x-rays.

Requests for medical reports should be honored promptly, as undue delays in providing medical reports or bills bearing on a patient's legal rights may prejudice the patient's rights.

If a physician is unable to state a complete medical evaluation and prognosis at the time it is required, he should so notify the lawyer and suggest to him that he request a further medical report at a later time. In such instances a preliminary report and medical bill, clearly designated as such, will often serve the patient's needs adequately.

E. The Interprofessional Conference

Personal conferences between the lawyer and each physician, whether he be an attending physician or an examining physician, are always proper and generally should be regarded as professionally obligatory.

Conferences should be scheduled at mutually agreeable times and under circumstances so that they may proceed without interruption.

Several conferences may be necessary. An initial conference long prior to trial and in some cases even prior to the commencement of a lawsuit is often desired by the lawyer so that he may be early apprised of the medical aspects of the claim, knowledge of which is, of course, essential to an evaluation of the claim. Interim conferences to discuss the patient's medical progress are often also necessary. If the physician is to be a witness, a final conference should be held as shortly as possible before the physician is to give testimony. At this conference the lawyer should explain the legal aspects of the case and the facts he expects to develop; and fully and with complete candor the physician should explain the medical aspects of the case. If a hypothetical question is to be asked, the lawyer should clearly outline it at the conference. The physician should review with the lawyer at the conference all his notes, records, memoranda and x-rays even though he does not intend to use them in his direct examination because they may be used in cross-examination. Before the conference concludes the physician should volunteer any pertinent medical fact not previously discussed.

Continued

F. Arrangements for Medical Testimony in Court

The lawyer should make arrangements with the physician who is to be a witness for the physician's appearance at a particular time and place and for the physician's testimony to be given as close to the specified time as possible. It is the obligation of the physician to be present at the specified time. The lawyer should give the physician as much advance notice of the specified time as is reasonably possible, but the physician must realize that the lawyer cannot control the court calendar and that unanticipated dispositions of preceding cases frequently prevent the lawyer from giving as much advance notice as might be desired. When a case is settled, the lawyer should promptly notify all physicians involved. Prompt notice is particularly important when a case is settled after a time for the physician's appearance in court has been set.

G. Subpoenas to Secure Medical Testimony

The lawyer should make every effort to arrange his client's medical evidence without the use of subpoena. In the event medical evidence cannot be obtained by arrangement, the lawyer may subpoena the physician. The physician must appear at the time requested and should not take offense at being subpoenaed. In the event a lawyer finds it necessary to subpoena a physician, the lawyer should notify the physician in ample time, preferably in advance of service of the subpoena, of his intention and insert in the subpoena a time for appearance as nearly as possible acceptable to the physician. A lawyer who subpoenas a physician should not expect the physician to bring with him his notes, records, memoranda and x-rays unless the physician has been served with a subpoena duces tecum.

Even though all physicians are experts in the eyes of the law, a physician can be compelled by subpoena to appear and testify upon tender to him of the statutory witness fees payable to any lay person who is subpoenaed. If a physician who appears in answer to a subpoena is examined with respect to any subject upon which he is an expert, the judge may at the conclusion of his testimony allow him a reasonable expert witness fee.

II. The Medical Witness at Trial

A. Appearance of Medical Witness

The proper, fair and impartial presentation of medical testimony is the joint responsibility of the physician acting as a medical witness and both examining lawyers.

The persons who are to hear and interpret the medical testimony, be it a jury, judge, or other presiding official, must necessarily observe and consider the appearance of the witness and presentation of the testimony. A medical witness should maintain a professional attitude in his appearance and should present his testimony in language that a layman can understand.

Our system of justice assumes that medical witnesses as well as other witnesses are impartial as to the facts within their knowledge. They are not and should not be advocates. A dogmatic, uncompromising, and argumentative attitude assumed by a witness instead of a firm but professional attitude based on honest convictions established on scientific principles will work to the detriment of the witness and as a result will work to the detriment of the patient on whose behalf he is testifying.

A lawyer should not engage in the abuse of any witness, including a physician, whether the witness be called by one side or the other. The established rules of evidence give ample opportunity for testing the competence and credibility of all witnesses, including a physician, making abusive examination on the part of a lawyer unnecessary and unjustifiable.

The physician should realize that it is the privilege and obligation of the lawyer for the opposing side to conduct his cross-examination with vigor in an effort to explore the foundations of medical opinion and to expose weakness which may appear in either the basis or content of such opinions. The physician should not be upset or assume an antagonistic attitude toward such cross-examination, providing the examining lawyer conducts it in a professional and gentlemanly manner. The physician must realize that such cross-examination is most probably based upon contrary medical interpretation of the objective facts known to all. A refusal to tolerate or to recognize a contrary view will not be in the best interests of the ad-

ministration of justice.

B. Medical Testimony

A physician should bring with him to court all his records with respect to the patient about whom he is testifying and may request that the hospital records with respect to such patient also be present in court. A lawyer should not counsel against the production of such records. When preparing to testify or when testifying a physician may examine such records to refresh his recollection. Once he has used them for such purpose, the lawyer for the opposing party may examine them too.

The qualification of a medical witness involves an inquiry into his medical education, post-graduate training and research and his membership in various medical organizations. The physician should be prepared to give a resumé of these professional qualifications without hesitation but without undue elaboration.

In the giving of testimony, the physician under no circumstances should permit any bias, prejudice, favoritism or personal interest to influence or affect his testimony. If the physician is asked a question to which he does not know the answer, he should so state and make no attempt to speculate or guess or theorize or give answers not responsive to the question propounded. A physician should not hesitate to express his opinions which are based upon a reasonable medical certainty. The medical witness is not required to exclude all doubts from his mind but may render his testimony as an opinion couched in expressions which fall short of an absolute conviction of accuracy. Simply because someone else might not agree with his opinions should not cause the physician to hesitate in expressing them. He must also remember that it is only fair that a contrary interpretation of the medical facts may exist and may be admitted. The physician must state his opinion if he has one. However, if he feels he is not qualified to give one, he should so state, and if he has no opinion he cannot be compelled to give one.

Trials are conducted according to rules of evidence and a physician may find that frequently during the presenting of his testimony there will be objections. These objections by the lawyers are merely a request to the court to

pass upon the materiality, the relevancy, or the competence of the testimony being offered. The court will rule according to the rules of evidence and the decision will be made as to whether the testimony should be considered along with other evidence in the case. The physician should not feel frustrated by these frequent interruptions since they are important and essential to protect the relative rights of the clients who are litigants.

It is frequently necessary to use hypothetical questions in eliciting testimony from medical witnesses. Such questions can be lengthy, troublesome and confusing if not properly prepared and presented. It is the lawyer's obligation to present such questions so as to be free from ambiguities and to eliminate any possible misunderstandings. The medical witness in attempting to answer the question, must, of course, be sure that he understands all of its elements and that they are sufficient and complete enough so that he can properly predicate his opinion thereon.

C. Ethical Limits of Medical Testimony

It is a rare occasion when intentional false or improper medical testimony is given in the trial of a case. However, it has occurred. Similarly, there are occasions when lawyers exceed the limits of propriety and attempt to introduce improper medical testimony or attempt to influence the testimony of the medical witness.

Each of the members of both professions has a duty to satisfy himself as a matter of conscience and professional judgment that the person doing so has exceeded the limits of ethical medical testimony or ethical handling of medical witnesses and once doing so has the obligation of reporting such activity to the appropriate organization within the profession which is set up to handle such matters.

The reputation of a professional person is his most precious and valuable asset. Therefore, the reporting of such improprieties against a member of one's own profession or against the member of another profession is a matter of great seriousness and calls for a high degree of discretion. It must be remembered that in an area such as medical testimony, there is a large degree of variance in opinions and in most cases these opinions are based

Continued

upon sound medical authority. The possibility of unintentional misstatements or representations also must be considered. Therefore, before any action is taken of any kind, the person doing so must be absolutely certain in his own mind and conscience that such action is warranted.

Conversely, it is just as serious to abstain from reporting such misconduct as it is to make a groundless charge. Therefore, when a member of either profession becomes convinced that such misconduct has occurred, it is his duty to report it.

III. Compensation of Medical Expert

A. Medical Fees

1. Contingent Fees

It is improper for the lawyer and the physician, whether he be an attending physician or an examining physician, to enter into any arrangement making the payment of medical fees, or the amount thereof, contingent upon the outcome of the litigation. Fixed fees should be established prior to the examination or court appearance.

2. Attending Physician

The expense of care and treatment of the patient is the obligation of the patient, irrespective of the litigation or the outcome thereof. The expense, if any, for preparation of medical reports for use by the patient's lawyer is the obligation of the patient. The expense of court appearance or preparation therefor is the obligation of the patient. The lawyer for the patient is under no legal obligation to pay such fees.

It is improper for the attending physician to insist, as a condition precedent to his testimony, that the lawyer for the patient guarantee payment of an unpaid bill for medical services, or bills for services to be incurred for the court appearance.

3. Examining Physician

The expense of an examination and report by an examining physician, as well as x-ray expense and similar costs necessary for a complete examination, are obligations in the first

instance of the lawyer requesting the same. Similarly, the expense of court appearance is an obligation in the first instance of the lawyer requesting the same. This fact does not relieve the client of his ultimate liability to pay the examining physician or reimburse his lawyer.

It is proper and desirable practice that whenever a lawyer refers a client to a physician for examination he should do so in writing, stating the terms of the reference. If the lawyer disclaims liability for the fee or if the physician doubts the lawyer's credit, the physician may be justified in withholding his report until the fee is paid or in declining to testify until mutually satisfactory financial arrangements have been made.

Payment of the examining physician's fees should be made promptly upon completion of his services. Delay in the final disposition, such as appellate procedure, is not sufficient reason for a lawyer to delay payment.

4. Court Appearances

The lawyer and his client should realize that a physician's fee for a court appearance is based upon many factors among which are not only actual time away from office but also stand-by time—i.e., the hours for which the physician has not been able to arrange a normal schedule of appointments either because he does not know exactly when he must appear in court or because he does not know exactly when he will return from court. They should also recognize that a physician is entitled to charge a fee for a court appearance if a case is settled while he is in the courtroom or if he has incurred stand-by time even though in either case he has not testified.

B. Professional Obligations of Attorney to Protect Physician for Fees on Services Rendered

In the event of recovery, the lawyer has an obligation to use all reasonable measures to assure payment by the client of the statement for services of the attending physicians, not only for the court appearance but also for services rendered. Whenever possible, unpaid statements should be satisfied as part of the process of distributing funds recovered in the litigation. A lawyer unable to make arrange-

ments for satisfaction of unpaid medical bills should promptly notify the physician of such facts.

Interprofessional Understanding

This code of interprofessional relations has been designed to promote better understanding between physicians and lawyers. If it is studied carefully and followed diligently by members

of both professions, it should go far to eliminate the frictions that have arisen and to enhance the areas of understanding. Improvement of the relationships between the two professions will enable the two professions to progress together in their service to humanity and its individual ills, whether of body, of mind, or to rights guaranteed under our system of justice.

Problems of Multiple-Handicapped Meeting

Plans are underway for a series of lecture and discussion meetings for Minnesota physicians on the problems of multiple-handicapped patients and how the creation of special diagnostic, evaluation and treatment centers throughout the state could aid these children, as well as the physicians whose patients they are.

Meetings are being scheduled for November 2 and 3 in Rochester, the Twin Cities and St. Cloud.

Speaker will be Dr. Richard Koch, chief of pediatrics at Children's Hospital, Los Angeles, Calif.; director of the Child Development Clinic at the hospital, and associate professor of pediatrics at the University of Southern California's School of Medicine, Los Angeles.

"Dr. Koch is widely known throughout the country as a pioneer in the establishment of these special Child Development Centers to help the child with the multiple handicap," said John Broady, St. Paul, executive director of the Minnesota Mental Retardation Planning Council.

Working with the Planning Council in sponsoring the meetings is the University of Minnesota's Department of Child Psychiatry. Other co-operating groups include: the Minnesota state department of education, division of special education; state department of health; state department of public welfare and its division of rehabilitation, child welfare and services to the blind; the Minnesota Association for Retarded Children; United Cerebral Palsy Association; Minnesota Society for Crippled Children and Adults, and the Easter Seal Society.

*O hour of all hours, most bless'd upon earth,
 Blessed hour of our dinners!
 We may live without poetry, music, and art;
 We may live without conscience and live without heart;
 We may live without friends; we may live without books,
 But civilized man cannot live without cooks.
 He may live without books—what is knowledge but grieving?
 He may live without hope—what is hope but deceiving?
 He may live without love—what is passion but pining?
 But where is the man that can live without dining.*

—Owen Meredith

Dr. Albert Einstein neatly summed up worry when asked if he ever worried about the future. "Why should I?" he answered calmly. "It gets here fast enough anyway."—Argosy.



The Arthritis Foundation salutes the thousands of dedicated physicians who volunteer their services in the nation's fight against crippling arthritis.

The Arthritis Foundation is the sole national voluntary health agency committed to conquering the rheumatic diseases. It provides the means for dynamic partnership between physicians and laymen to marshal leadership and resources toward the solution of this major national health problem.

The Arthritis Foundation looks forward to rapid growth with increasing opportunity for physicians to participate in the arthritis movement. For further information about The Arthritis Foundation and its programs write to the Foundation chapter in your community or to the Medical Department, Box 2525, New York, N.Y. 10001.

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Minnesota Medicine at a Glance

Paradox of Brucellosis—*MacDonald et al.*

Page 1469.

The authors discuss the current brucellosis scene. The classification they find most useful divides cases into bacteremic, serologic, localized and mixed types. The current antibiotic regimen of reference is a combination of tetracyclines and streptomycin. Emphasis is placed on surgical drainage of suppurative brucellar infections.

Farm Accidents—*Muckala*

Page 1477.

We in Minnesota have no functioning Agricultural Extension Safety Division concerned with safety education, promotion and design. It is essential for a major agricultural state and a major university medical center to have a professional group, or institute, to concern itself with the epidemiological aspects of rural health and farm safety. It can also function as a source of information and education for the professional portions of our rural communities who are directly concerned in health promotion and preventive medicine.

Polymyalgia Rheumatica—*Nuessle et al.*

Page 1483.

A cluster of findings, including muscular pain, high sedimentation rate, ocular symptoms, and occasionally giant cell arteritis of temporal vessels is described in seven cases. The syndrome, entitled polymyalgia rheumatica, appears in old women and is considerably relieved by steroid therapy.

Bacteremia and Candida Septicemia—*Salter and Zinneman*

Page 1489.

The authors have reviewed 185 cases of bacteremia and fungemia seen at the Minneapolis Veterans Administration Hospital in a four-year period between 1962 and 1965. They found a high incidence of coagulase positive staphylococci and *Escherichia coli*. The most common gram-negative organisms were *Proctus* and *Klebsiella enterobacter*.

In the first year of the study *Candida* was present in 4.6 per cent of the total number of positive cultures, but in the last year of the study was present in 11.9 per cent. The urinary tract was the most common source of non-fatal bacteremias, followed by respiratory tract. But in fatal bacteremias this was reversed. The most important factor associated with the positive blood culture was the presence of other disease, particularly neoplastic disease and especially of the hematopoietic system. Diabetes mellitus, gastrointestinal, biliary tract disease, chronic lung disease and genitourinary tract disease were underlying conditions. The intravenous pyelogram polyethylene catheter is a frequent portal of entry. Shock during the course of bacteremia was associated with a mortality of almost 60 per cent.

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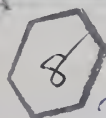
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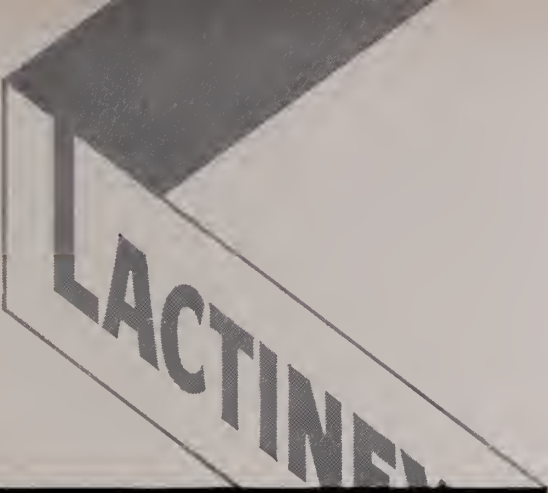
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References:

- (1) Siver, R. H.: CMD, 21:109, September 1954. (2) Frykman, H. H.: Minn. Med., 38:19-27, January 1955. (3) McGivney, J.: Tex. State Jour. Med., 51:16-18, January 1955. (4) Quehl, T. M.: Jour. of Florida Acad. Gen. Prac., 15:15-16, October 1965. (5) Weekes, D. J.: N.Y. State Jour. Med., 58:2672-2673, August 1958. (6) Weekes, D. J.: EENT Digest, 25:47-59, December 1963. (7) Abbott, P. L.: Jour. Oral Surg., Anes., & Hosp. Dental Serv., 310-312, July 1961. (8) Rapoport, L. and Levine, W. I.: Oral Surg., Oral Med. & Oral Path., 20:591-593, November 1965.

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President's Letter

ALL THE PHYSICIANS of Minnesota, especially the General Practitioners or Family Physicians, have lost, at least temporarily, a stalwart champion in the University of Minnesota Medical School. I do not mean to imply that he is the only one there who has the great interest of this group in mind, but, in my humble opinion, he is oriented to both "patient care" and General Practice. Such a man is Dr. Richard M. Magraw. He has taken sabbatical leave to serve as Consultant to the Surgeon General, and especially to the Bureau of Health Services.

Dr. Magraw has labored for years with his Comprehensive Clinics at the University Medical Center. He sprang into national prominence with the publication of his very excellent book, "Ferment in Medicine," which came out this past year and should be a MUST for every physician to STUDY. I read fairly rapidly, but I couldn't go through this book in a hurry and am in the process of restudying it now.

It is my hope, and I think I can safely say that this hope is shared by the great majority of physicians in the state, that he could be replaced by someone with the same dedication to the principles for which he stands. It would seem reasonable to assume that the "talked about" new department of General Practice, or whatever it is to be called, could somehow be developed from these Comprehensive Clinics. Its head must be a strong individual, capable of withstanding much storm and strife, because he will be shot at from all directions, I would predict, and it will be very difficult for him to make this department into a "going" concern. Now is the time when Dr.

Magraw should be really getting into stride here, because he has the background and intestinal fortitude to develop such a department.

I say this with as much kindness as I can, and without meaning to be cynical. Years ago the entire Medical School faculty was "patient care"-oriented, because research was in its infancy. As time has passed, it is very understandable that it should swing more and more into the "research"-oriented orbit, along with the tremendous burgeoning of our total scientific effort. During this process, however, the "patient care" attitude has suffered and become somewhat of a stepchild of academic medicine.

It is obvious that both viewpoints are required; the problem is one of emphasis. We are "off trajectory," as it were, and any re-orientation must necessarily come through the combined efforts of those supporting both points of view. Such reemphasis *must be accomplished* by the cooperation of the entire faculty, as well as the Metropolitan Community in which it is situated. I would guess that the great majority of the faculty is more "research"-oriented than "patient care"-oriented. Of necessity, research cannot be neglected, but more emphasis must be placed on teaching the students to be practitioners of medicine. It should certainly be possible to combine the two, as most research should be aimed at improvement of health, rather than being "pure" research, which so much of it seems to be at the present time.

If any of the faculty wishes to dispute these statements, I would be pleased to see a "Letter

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Diverticular Disease of the Colon

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IN THE LAST few years, investigators in England and Sweden have clarified the concepts of etiology and pathophysiology of diverticular disease. The function of the normal sigmoid colon has been better defined and contrasted to an altered function in diverticular disease. On the basis of these studies, a relationship between the irritable colon syndrome and diverticular disease can now be suggested.

Etiology and Pathogenesis

Understanding of the development of diverticula has been obscure until recent years. Weakness of the muscle layer of the colon has been thought responsible, as has increased intraluminal pressure. Several objective studies have now shed some light on the pathogenesis of diverticula.

Alteration of Intraluminal† Pressure

Pressure in the rectosigmoid can now be recorded by placement, through a proctoscope, of fluid-filled tubes connected to a manometer, and this relatively new technique has provided considerable new data.

Quantitative Measurement of the Intraluminal Pressure

The intraluminal pressure and the degree of muscle activity in the sigmoid colon have been studied in normal volunteers and compared with those in patients who had evidence of diverticular disease of the colon. This was done by Arfwidsson in Sweden¹ and Truelove and his school in England.²⁻⁸

In measurements at rest, Arfwidsson¹ found about a five-fold increase in total muscle activity in patients with diverticular disease as compared with healthy subjects. In addition, there were more waves reflecting high pressure in the patients with diverticular disease; and complex waves were present that did not occur in normals. On the other hand, Painter and True-

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†See Test Your Word Score Page 1659.

love,² using the same technique but a different method of analysis, did not find a statistically significant difference between these groups.

In postprandial measurements, both Arfwidsson's and Truelove's groups observed that after a meal the intraluminal pressure in the sigmoid was increased in both normals and patients with diverticular disease, but to a much more marked degree in the latter.^{1,8}

The effect of various drugs has been studied. Neostigmine (Prostigmin) was found by both groups^{1,4,6} to increase markedly the intraluminal pressure in both the normal and the diseased colon, but again to a much more marked degree in the diseased state. Morphine was found by Painter and Truelove³ to have the same effect. Meperidine (Demerol), on the other hand, did not have this action; it depressed the muscular activity of the colon.⁵ In one study, analysis of patients hospitalized for diverticular disease disclosed three cases in which perforation of the bowel was attributed to the administration of morphine.⁶ These studies are the basis for the recent recommendation to avoid the use of morphine in diverticular disease of the colon and to control pain when necessary with meperidine.

Propantheline (Pro-Banthine) inhibits the motility of the colon and can prevent morphine-induced contraction when the drugs are given simultaneously.⁵

Effect of Increased Intraluminal Pressure: Genesis of Diverticula

The studies just referred to demonstrate that the intraluminal pressure of the colon in diverticular disease can be quite high. How can this lead to the development of diverticula?

The musculature of the human sigmoid colon has certain peculiarities which may explain how a high intraluminal pressure can be quite localized. The muscle wall consists of two layers. Three longitudinal taeniae constitute the outer layer; one is located at the mesenteric border and two are at the antimesenteric border. The latter come quite close to each other in the region of the sigmoid. The inner circular muscle is fasciculated—that is, grouped in bundles. This lack of continuity helps explain the genesis of diverticula. Both muscle layers are attached to each other at their junctional surface, so that contraction of the taeniae produces crowd-

ing of the circular bundles, shortening of the sigmoid, and, more important, partial segmentation of the sigmoid. Two localized contractions of the circular bundles can now occlude the lumen completely at each end of a segment of sigmoid; and if the intervening circular muscle of the segment contracts, a very high pressure is generated.

Pressures of considerable magnitude were often found to be localized.^{2,7} Pressure-recording devices were placed at different levels in the rectosigmoid, and the motility patterns registered were without relation to each other in time or in intensity. However, only those leads related to diverticula recorded increased pressures. When cineradiography was combined with pressure recording, it was seen that the colon-bearing diverticula functioned as a series of separate segments and that distention of the diverticula occurred when the related segments contracted.⁷

It has been argued that the increased intraluminal pressure is the consequence and not the cause of diverticular disease. However, Arfwidsson has described several patients with a prediverticular condition in which the intraluminal pressure is increased but without associated diverticula.

What Produces an Abnormal Motility Pattern?

Because of a marked predominance of sympathetic activity, the colon is normally fairly relaxed.⁹ There is evidence in some subjects that stress alters this condition;¹⁰ pain, induced hypoglycemia, and physiologic trauma have been shown to increase markedly the motility of the sigmoid.

A study of patients with the irritable colon syndrome discloses differences from the normal relaxed state of the colon. Such patients can be divided into two groups:¹¹ those who have a "spastic" colon manifested by pain that occurs mainly along the course of the left colon, and more rarely, those having painless diarrhea. Reaction to stress in both groups of individuals is of greater intensity and duration than in the normal.¹⁰ Pressures recorded in the same manner as described above showed normal patterns in the absence of symptoms, a decrease in activity in the diarrhea group when they had symptoms, and an increase in the group having pain.¹²⁻¹⁴ In the last-named,

segmental contraction like that seen in patients with diverticular disease was seen by cinefluoroscopy and could be abolished by propantheline.¹¹ In both forms there is an abnormal increase in motility in response to neostigmine (Prostigmin)^{11,12} and meals.¹⁵ No prospective or retrospective study is available as yet to link the irritable colon syndrome—a presumed psychosomatic condition—to diverticular disease—an organic disease. However, from what has just been described, the analogy is striking and the bulk of evidence now points to a possible relationship. Occasionally, it is possible to follow the development of diverticula superimposed on a spastic colon.¹⁶

Influence of Diet

The chronic feeding of rats with a low-residue diet produced diverticula; this did not occur in a group fed a normal diet.¹⁷ No diverticula are present in Africans living tribally in Africa.^{7,18} Their diet is high in bulk. Among their American cousins there has been a steady increase in diverticular disease in the last 50 years coinciding with a reduction of the residue in their diet. Virtual absence of diverticulosis has been reported in Korea, where the diet is composed of a large proportion of high-residue elements.¹⁹

Such evidence allows a basis for revision of our traditional concepts of diet in diverticular disease. The use of the low-residue diet in the irritable colon syndrome and for patients with diverticular disease would not appear justified on the basis of the above evidence. It would seem more reasonable to avoid obliteration of the sigmoid lumen when possible, and a diet high in residue may afford some protection in this regard.

Although in most cases of diverticular disease of the colon, the sigmoid is involved and progression occurs orad from there, some diverticula can occasionally be demonstrated in the transverse colon or the right colon without involvement of the left side.^{1,7,20,21} In the sigmoid, the lumen normally is smaller and the muscle thicker than elsewhere in the colon, and this may explain the frequency of its involvement with diverticula.^{1,22,23}

Pathology

The Diverticulum

Acquired diverticula of the colon are usually

located between the taeniae of the mesenteric border and those of the antimesenteric border. In the advanced stage of the disease, a few smaller ones may appear between the latter.^{16,24} Dogs have no taeniae but a continuous longitudinal sheet, and diverticula in these animals never develop. Perhaps for the same reason the human rectum is free of this disease.

Microscopically, the diverticulum is usually formed by a mucosal outpouching along the blood vessel pathways piercing the circular muscle.

As noted previously, prediverticula have been demonstrated by Arfwidsson.¹ He studied two patients who had symptoms of pain in the left lower quadrant, the typical saw-tooth pattern of the sigmoid on x-ray study, and a motility recording like that described above. Both patients underwent resection of the sigmoid, and in each the ends of the sigmoid were tied off after the specimen had first been filled with formalin to a pressure of 60 cm. of water. After two days in a formalin bath, the specimens were examined. Tiny diverticular precursors were found which were described as outpouchings of the submucosa along the vessel pathways. For these the term incomplete or intramural diverticula has been coined.²⁵

Some authors have called attention to the fact that to have symptoms it is not necessary to have inflammation of the diverticula^{1,16,26-28} or to have a mass palpable clinically or at surgery. In one series²⁷ 30% of specimens from patients operated on for diverticulitis did not have any sign of inflammation. Arfwidsson¹ found no inflammation in eight of 29 specimens. Morison²⁷ in England and Fleishner and associates¹⁶ from Harvard are in agreement with these findings.

It is postulated that once the mucosa has been damaged, infection can occur and extend toward the pericolic fat and the peritoneum. The mucosa adjacent to the diverticula is rarely affected.¹

Chronic infection of the mucosa of the diverticulum results in the formation of granulation tissue²⁷ and can cause the ulceration of an arteriole²⁹ with resultant bleeding.

Colon Musculature

The musculature of the colon may be remarkably thickened in diverticular disease.

Statistical analysis shows true hypertrophy rather than hyperplasia,¹ but this has recently been challenged.³⁰ Pleating of the wall also occurs,^{1,16,27,28} and microscopic examination reveals that it involves not only the mucosa along the taeniae but also the whole wall in between them. Stripping the taeniae¹⁶ permits stretching of the specimen beyond its normal size, and this shows the importance of the taeniae in the genesis of the pleating. Cineradiography⁶ has shown that despite the increased thickness of the muscle, the neck of the diverticulum was not shut off during contraction.

Colon Fat

Increase in fat may be more apparent than real and represent the crowding of the bowel by spasm.^{27,31}

Symptomatology

Although classically diverticulosis has been held as asymptomatic, the noninflammatory stage of the disease may in fact be related to some of the symptoms previously attributed to diverticulitis.²² Pain and symptoms from intermittent partial obstruction do not necessarily indicate infection, nor does a tender mass in the left lower quadrant. Only fever and peritoneal irritation can be securely related to inflammation together with leukocytosis and elevation of the erythrocyte sedimentation rate.

Proctoscopic Examination

In diverticulosis the bowel may be fixed and angulated, and occasional diverticula may be seen. These can be inverted and they may simulate a polypoid lesion. To this picture edema and erythema of the mucosa may be added in diverticulitis.

Roentgenologic Examination of the Colon

Barium at times flows in with difficulty both in irritable colon syndrome¹¹ and in diverticular disease. A saw-tooth pattern on the x-ray film is typical of both diseases;^{1,22} the lumen of the sigmoid is smaller than usual and is segmented by deep indentations of the colonic wall.^{7,11,16} When present, diverticula are located at the top of the haustra between these contraction rings. Postevacuation films often

show retention of barium in diverticula or segmented pockets of colon.

Exclusion of carcinoma on a roentgenologic basis can be difficult. As a rule, diverticular disease involves a longer segment with normal mucosa and without short abrupt edges; fluoroscopy may demonstrate spasm²¹ in diverticular disease.

Fistulas or communication with an abscess can sometimes be demonstrated on postevacuation films after an acute episode.²¹

Finally, if barium enema is necessary in acute diverticulitis, caution should be used to avoid perforation.

Treatment

Medical Treatment

Two main points have to be emphasized. One is the suggested avoidance of morphine and its replacement by meperidine for control of severe pain. The other is the use of a high-residue diet and bulk-forming laxatives in both irritable colon syndrome and diverticular disease.

In cases of acute diverticulitis, bed rest, sedation, propantheline, antibiotics by mouth or parenterally, and local heat should be instituted.

Surgical Treatment

Indications.—Only 5% of patients who have diverticular disease undergo surgery. For many years surgical treatment was limited to the treatment of the complications: perforation, fistula, obstruction, and uncontrolled bleeding. In addition, acute diverticulitis associated with high mortality has been reported to occur in patients who have had no previous episodes,³² and in these patients resection was eventually undertaken. Arfwidsson has recommended that the association of high intraluminal pressure, typical x-ray pattern, and intractable symptoms be regarded as surgical indication. In some instances, the impossibility of excluding carcinoma is also a surgical indication.

Surgical Techniques

A trend has developed to replace the classic three-stage procedure (colostomy-resection-closure of colostomy) by the one-stage resec-

tion without colostomy.^{31,33-35} It was shown that the one-stage operation carries less morbidity and the same operative mortality.³⁶ One randomized study, grouping all perforated lesions of the colon, is available and shows a higher mortality and morbidity in the multiple-stage group.³⁷ Surgical resection is followed by virtual absence of recurrence.^{31,33,35}

Sigmoid myotomy has been devised by one author to attack the problem at a more physiological level.³⁸ An incision of six inches or more, carried from the peritoneal surface to the level of normal colonic mucosa,³⁹ is made along the antimesenteric taeniae, cutting all circular muscle. Time will tell the usefulness of such procedures.

Summary

Thanks to recent studies, we now understand more of diverticular disease of the colon and have a meaningful concept of its cause, pathogenesis, and physiology. Our recommendations can now be more rational. Of importance is the avoidance of morphine, its replacement by meperidine and propantheline, and the usefulness of a high-residue diet.

Diverticulosis, previously thought harmless, has been found in some cases to be associated with symptoms.

The one-stage resection is becoming the procedure of choice for surgical treatment.

References

1. Arfwidsson, S.: Pathogenesis of Multiple Diverticula of the Sigmoid Colon in Diverticular Disease. *Acta Chir Scand Suppl* 342:1, 1964.
2. Painter, N. S., and Truelove, S. C.: The Intraluminal Pressure Patterns in Diverticulosis of the Colon. Part I. Resting Patterns of Pressure. *Gut* 5:201, 1964.
3. Painter, N. S., and Truelove, S. C.: The Intraluminal Pressure Patterns in Diverticulosis of the Colon. Part II. The Effect of Morphine. *Gut* 5:207, 1964.
4. Painter, N. S., and Truelove, S. C.: The Intraluminal Pressure Patterns in Diverticulosis of the Colon. Part III. The Effect of Prostigmine. *Gut* 5:365, 1964.
5. Painter, N. S., and Truelove, S. C.: The Intraluminal Pressure Patterns in Diverticulosis of the Colon. Part IV. The Effect of Pethidine and Probanthine. *Gut* 5:369, 1964.
6. Painter, N. S., Truelove, S. C., Ardran, G. M., and Tuckey, M.: Effect of Morphine, Prostigmine, Pethidine, and Probanthine on the Human Colon in Diverticulosis Studied by Intraluminal Pressure Recording and Cineradiography. *Gut* 6:57, 1965.
7. Painter, N. S., Truelove, S. C., Ardran, G. M., and Tuckey, M.: Segmentation and the Localization of Intraluminal Pressures in the Human Colon, With Special Reference to the Pathogenesis of Colonic Diverticula. *Gastroenterology* 49:169, 1965.
8. Truelove, S. C.: Movements of the Large Intestine. *Physiol Rev* 46:457, 1966.
9. Bennett, A., and Whitney, B.: A Pharmacological Study of the Motility of the Human Gastrointestinal Tract. *Gut* 7:307, 1966.
10. Almy, T. P., Kern, F., Jr., and Tulin, M.: Alterations in Colonic Function in Man Under Stress. II. Experimental Production of Sigmoid Spasm in Healthy Persons. *Gastroenterology* 12:425, 1949.
11. Lumsden, K., Chaudhary, N. A., and Truelove, S. C.: The Irritable Colon Syndrome. *Clin Radiol* 14:54, 1963.
12. Chaudhary, N. A., and Truelove, S. C.: Human Colonic Motility: A Comparative Study of Normal Subjects, Patients With Ulcerative Colitis, and Patients With the Irritable Colon Syndrome. *Gastroenterology* 40:1, 1961.
13. Ritchie, J. A., Ardran, G. M., and Truelove, S. C.: Motor Activity of the Sigmoid Colon of Humans: A Combined Study by Intraluminal Pressure Recording and Cineradiography. *Gastroenterology* 43:642, 1962.
14. Wangel, A. G., and Deller, D. J.: Intestinal Motility in Man. III. Mechanisms of Constipation and Diarrhea With Particular Reference to the Irritable Colon Syndrome. *Gastroenterology* 48:69, 1965.
15. Mielke, J. E., Becker, K. L., and Gross, J. B.: Diverticulitis of the Colon in a Young Man With Marfan's Syndrome: Associated with Carcinoma of the Thyroid Gland and Neurofibromas of the Tongue and Lips. *Gastroenterology* 48:379, 1965.
16. Fleischner, F. G., Ming, S.-C., and Henken, E. M.: Revised Concepts on Diverticular Disease of the Colon. I. Diverticulosis: Emphasis on Tissue Derangement and Its Relation to the Irritable Colon Syndrome. *Radiology* 83:859, 1964.

17-39 may be secured from the author or the reprints.

Man is a gregarious animal, and apparently the mischievous microbes he exhales fight and neutralize each other. They go out and devour each other, and Man walks off unharmed. If this is not scientifically correct, it ought to be.

—Winston Churchill

Count that day won when, turning on its axis, this earth imposes no additional taxes.

—Franklin Adams

Acupuncture*

An Ancient Chinese Practice

"That a needle stuck into one's foot should improve the functioning of one's liver is obviously incredible. It can't be believed because, in terms of currently accepted physiological theory 'it makes no sense.' Within our system of explanation there is no reason why the needle-prick should be followed by an improvement of liver function. Therefore, we say it can't happen.

"The only trouble with this argument is that, as a matter of empirical fact, it does happen. Inserted at precisely the right point, the needle in the foot regularly affects the function of the liver."**

Just where is that "right point"? On a diagram of the human figure it is labeled Liv 2 and is situated on top of the right foot between the first and second toes. How can it be precisely determined? The acupuncturist expertly glides a sensitive finger along the liver meridian (circuit) which, in a case of suspected liver disease, responds with a tender pulsation at the exact spot for the insertion of the needle. Such acupuncture at Liv 2 sedates the liver when it is overcharged with Qi (energy).

If, however, the liver is deficient in Qi, tonification is required and is achieved at Liv 8, a point on the inside of the right leg near the knee.

Similarly, all malfunctioning organs undergo therapy at special points along their respective meridians to increase or decrease their energy flow. Startling to behold is a diagram of man's body designating the minute areas for needle insertion along the 12 meridians!

There are 365 such strategic spots located on the head, body, and extremities. The needles are made of various metals, come in different shapes and sizes, and are pushed into the tissue by a rotary motion to propitious depths, being left there however long the acupuncturist considers feasible—from a few minutes to as much as an hour.

Deceptively simple as the theory of acupuncture may appear, it is amazingly complex, operating under manifold laws, the four major ones being the Mother-Son law, the Husband-Wife law, the Midday-Midnight law, and the Five-Elements law. These laws govern the intricate amphoteric interaction of organ stimulation and sedation, since acupuncture affects not only the single organ being treated but also the neighboring organs on the same meridian.

In ancient China acupuncture was the traditional routine in the practice of preventive medicine. The physician checked up on his regular clients periodically by deftly running his finger along their meridians and noting subtle responses that indicated incipient disease before overt symptoms appeared.

Acupuncture, long confined to China, recently disseminated itself in Western Europe, particularly in France and Germany in the 1930s, where it is still being practiced in conjunction with conventional medicine, chiefly to relieve rheumatic disorders.

According to the Encyclopedia Britannica, however: "There is no known physiologic basis to acupuncture."

Which is not to deny that there might be an as yet *unknown* basis!

*See Test Your Word Score Page 1659.

**Aldous Huxley in his Foreword to Felix Mann's *Acupuncture*, 1962.

Aortic Stenosis and Unexplained Gastrointestinal Bleeding

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IN 1958, Heyde and Schwartz,^{1,2} reported for the first time the association between aortic stenosis and profuse recurrent gastrointestinal bleeding from an unknown site. Since then other cases of this perplexing clinical problem have been reported in the literature. Our patient with typical aortic stenosis had twelve hospital admissions for gastrointestinal bleeding.

Case Report

This 71-year-old white male was first admitted to Northwestern Hospital, Minneapolis, Minnesota, on January 8, 1964, complaining of weakness, shortness of breath, melena of three months duration and a syncopal episode one day prior to admission.

On physical examination his blood pressure was 160/90, pulse rate 88 per minute and weight 185 pounds. There was slight cardiac enlargement to the left and a loud harsh ejection systolic murmur heard best over the aortic region radiating to both carotid areas indicative of aortic stenosis. A diastolic murmur was not heard.

The admission hemoglobin was 9.8 grams per cent, SGOT 22 units, hematocrit 32.5 per cent, platelets 553,000 per cu. mm., prothrombin time 13.9 with a control of 12.2 seconds, Lee-White clotting time 11 minutes, and Ivy bleeding time three minutes. The electrocardiogram was compatible with a left ventricular hypertrophy. Upper gastrointestinal x-ray series showed a questionable deformity of the duodenal bulb, and a barium enema revealed large numbers of diverticula. The stools were black and Guaiac-positive for blood.

Surgical exploration of the abdomen was carried out in an attempt to establish the site and etiology of the bleeding. No blood was found in the small intestine but a rather large amount in the large intestine. Since the patient had rather extensive diverticulosis involving the entire colon, *a colectomy with an ilioproctostomy was performed.* Prior to surgery the patient received six units of blood and following surgery four units. He did well after surgery and was discharged on February 23, 1964, with a hemoglobin of 12.6 grams per cent.

The *second admission* occurred on April 20, 1964, because of tarry black stools and weakness. Physical examination was essentially normal except for the murmur of aortic stenosis. Admission hemoglobin was 9.5 grams per cent and the stool guaiac 4+. Stomach and small bowel x-rays were essentially normal as was esophagoscopy and the Einhorn string test. Over the next several days the patient was given three units of blood and discharged on April 24, 1964, with a hemoglobin of 13.5

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grams per cent.

The *third admission* was on June 2, 1964, for repair of an incisional hernia. The hemoglobin was 11.3 grams per cent.

The patient was *admitted for the fourth time* on July 8, 1964, with the complaint of weakness, faintness and an occasional dark stool. Physical examination was essentially unchanged. The admission hemoglobin was 7.8 grams per cent, the hematocrit 23 per cent and the stool guaiac 4+. Stomach and small bowel x-ray examination was essentially normal, and the Einhorn string test did not localize a site of active hemorrhaging. A transfusion with two units of blood was given and he was discharged on July 11, 1964, with a hemoglobin of 13.1 grams per cent.

The patient was *hospitalized for the fifth time* on September 22, 1964, with the complaints of weakness, faintness and dark stools. His admission hemoglobin was 9.4 grams per cent with a 4+ stool guaiac. Stomach x-ray revealed a gastric diverticulum and a possible duodenal ulcer.

Four units of blood were given preoperatively. At surgery, a large gastric diverticulum and a small posterior wall duodenal ulcer were found. A *subtotal gastrectomy* was performed and, in addition, cholecystectomy for cholelithiasis was carried out. The patient's recovery was uneventful, and he was released from the hospital on October 7, 1964, with a hemoglobin of 12.2 grams per cent.

The *sixth admission* was February 16, 1965, for a complaint of diarrhea. No definite cause could be found for his diarrhea other than probable intestinal insufficiency. This admission was complicated by a gram-negative bacteremia with shock for which he was treated and recovered. His hemoglobin values dropped from 11.8 to 8.8 grams per cent, necessitating two transfusions. The patient was discharged March 3, 1965.

The *seventh admission* was March 6, 1965, for crampy abdominal pains and vomiting. Flat plate of the abdomen revealed distended loops of bowel. The patient was treated conservatively for partial small bowel obstruction. His recovery was rapid, and he was discharged on March 9, 1965.

The *eighth admission* was July 8, 1965, for the complaints of weakness and dark stools. The admission hemoglobin was 8.4 grams per cent, and he had a 4+ stool guaiac. A string test suggested multiple minimal bleeding sites. The patient was transfused with two units of packed cells and discharged July 14, 1965, with a hemoglobin of 11.8 grams per cent.

The *ninth admission* was July 15, 1965, for dark stools. Admission hemoglobin was 10.6 grams per cent. The patient was treated with intramuscular iron dextran (Imferon) and discharged on July 17, 1965.

The *tenth admission* was September 28, 1965, for weakness and dark stools. The admission hemoglobin was 7.8 grams per cent and the stool guaiac 4+. Over the following week he received five pints of blood. He was discharged on October 3, 1965, with a hemoglobin of 11.7 grams per cent.

The *eleventh admission* was June 8, 1966, for dark stools. The admission hemoglobin was 9.2 grams per cent, and he had a 4+ stool guaiac. He received three

units of blood. His hospital course was complicated by a urinary tract infection. On discharge his hemoglobin was 13.3 grams per cent.

The *twelfth admission* was July 7, 1966, for chills and fever of two days duration. Physical examination was essentially unchanged. Blood cultures revealed alpha Streptococcus. A diagnosis of subacute bacterial endocarditis was made. He was treated with 20 million units of intravenous crystalline penicillin per day for six weeks. Shortly after institution of therapy, the patient developed a grade III/VI diastolic blowing murmur along the left sternal border. During his hospital stay, he received two units of blood because of continued occult bleeding. He was discharged August 7, 1966, with the diastolic blowing murmur of aortic insufficiency barely audible. He was well without bleeding up to April 1967.

Discussion

Heyde¹ reported that during a ten-year period he had seen ten patients with calcific aortic stenosis and associated gastrointestinal bleeding of undetermined origin. All patients were between 60 and 80 years of age. Schwartz² cited several other patients with calcific aortic stenosis and gastrointestinal bleeding.

The largest series was reported by Williams³ in 1961. He analyzed a group of 1443 patients with gastrointestinal bleeding and found that 1348 patients (93.5 per cent) had a demonstrable cause for their bleeding, and 5 per cent of them had aortic stenosis. Matched controls showed an incidence of 4.4 per cent. Of these 95 patients with unexplained bleeding 25.5 per cent had an aortic valve lesion, mainly calcific aortic stenosis. Among age and sex-matched controls admitted during this same period, aortic stenosis was present in 5.2 per cent. Therefore there was nearly a five times greater incidence of aortic stenosis in those patients with unexplained gastrointestinal bleeding. Of those individuals with aortic valve lesions, 17 per cent had a positive test for syphilis, 25 per cent had evidence of diabetes mellitus, and most were in the 7th and 8th decade of life. Laboratory studies demonstrated no consistent or gross abnormality by which the gastrointestinal hemorrhaging could be explained.³

Since William's report, other scattered case reports have appeared in the literature. Castleman⁴ described a 78-year-old female who had multiple admissions for gastrointestinal bleeding associated with calcific aortic stenosis. Trowbridge⁵ reported a series of four cases with undetermined gastrointestinal bleeding

and aortic stenosis.

The etiology of gastrointestinal bleeding is not known. Williams³ mentioned several interesting possibilities. He speculated that prolonged diminution of left ventricular output and consequent tissue hypoxia might be the cause for profuse gastrointestinal bleeding. Calcific aortic stenosis may be associated with visceral arteriosclerotic vascular disease, thus predisposing the intestinal tract to bleeding from minimal physiologic trauma such as food and alcohol. It is of interest that most of our patient's episodes of gastrointestinal bleeding were associated with excessive alcoholic intake and/or eating such foods as peanuts. Syphilitic endarteritis in the mesenteric bed could be a cause. In Williams' study there was no pathological material to test this

latter hypothesis.

Summary

This is a case report of a 71-year-old white male with calcific aortic stenosis and repeated episodes of gastrointestinal bleeding from an undetermined site. The patient was hospitalized 12 times, underwent three surgical procedures, and received 35 units of blood. It appears that the combination of aortic stenosis and unexplained repeated gastrointestinal hemorrhage is not just coincidental. It is speculated that tissue anoxia and mucosal fragility from the lowered cardiac output in aortic stenosis, the arteriolar insufficiency of visceral arteriosclerosis, and syphilitic endarteritis are attractive etiological possibilities in this perplexing problem.

References

1. Heyde, E. C.: Gastrointestinal Bleeding in Aortic Stenosis, Correspondence. *New Engl J Med* 259:196, 1958.
2. Schwartz, B. M.: Additional Note on Bleeding in Aortic Stenosis, Correspondence. *New Eng J Med* 259:456, 1958.
3. Williams, R. C.: Aortic Stenosis and Unexplained Gastrointestinal Bleeding. *Arch Intern Med* 108:859, 1961.
4. DeSanctis, R. W.; Castleman, Benjamin: Chronic Melena and Bacteremia in a Patient with a Cardiac Murmur. *New Engl J Med* 273:1096, 1965.
5. Trowbridge, Mason: Aortic Stenosis and Gastrointestinal Hemorrhage: Report of Four Cases. *J Maine Med Ass* 56:276, 1965.

It's the Law

Hospital Parking Lot Exempt from Taxation

A trial court granted a hospital's application for declaration that its parking lot was exempt from taxation. The parking lot was built for the sole purpose of providing off-street parking for patients, employees and visitors only, and some effort was made to limit public use of it. Employees were issued cards which admitted them to the lot free of charge. Others paid a fee of 25¢. There was testimony that visitations were considered supportive therapy for patients. If a visitor were unable to pay the 25¢, he would be permitted to park free of charge.

The operation of the lot had resulted in some profit. However, it was clear that the hospital's purpose in operating the lot was not to make a profit, but to provide necessary services and facilities. Thus, its operation was incident to the hospital's major purpose, and the lot was, therefore, exempt from taxation.*

*Case Reference—*Ellis Hospital v. Fredette*, 279 N.Y.S. 2d (N.Y., May 15, 1967). *The Citation*, Vol. 15, No. 9, August 15, 1967.

The advance of scientific knowledge as it really happens is not a steady resolute march to the stars. It goes something like this: One step forward, two steps sideways, fall flat on your face. Get up facing backwards, and try to see which way you were going; then repeat da capo.

—Daniel Luzon Morris

Blood-letting

The body had three doors through which it could evacuate noxious matter: through the skin in the form of sweat, through the kidneys as urine and through the bowels as feces. But since there were four juices there must also be four exits. The doctors invented this fourth door in the shape of blood-letting.

Hippocrates first gave blood-letting, within the framework of the juices theory, a scientific foundation; it was held to be the last means of driving the sick juices from the body when sweating, purging and diuretics failed.

In Paris at the turn of the nineteenth century patients were unscrupulously bled. Bleeding from countless incisions, they lay there like the victims of some blood-thirsty sacrifice so exhausted by the heavy loss of blood that they were hardly able to groan. The wounds often became infected and suppurated, so that the sick often died of dermatitis. It was heralded as a great step forward when Broussais conceived the idea in minor cases of blood-letting painlessly with the aid of leeches rather than by opening the veins.

Now it became the fashion, it was believed that the leech was capable of sucking all the deleterious* matter from the body. The demand for these creatures was enormous. Soon every pond in France had been scoured of these valuable worms, and they had to be imported from Bohemia, Hungary and the Baltic countries. Between 1827 and 1836 the Paris hospitals alone used five to six million leeches annually at a cost of a million and a half francs.

France alone needed in the neighborhood of thirty-three million leeches. They lay in readiness in rows of glass containers. The leeches were placed on the belly of the patient in order by their powers of suction to relieve the excess blood of gastroenteritis. Applied in their hundreds they sucked the patient's belly until it looked like a black glittering coat of mail. Full of hope, doctors and patients alike watched the silent activity of their little helpers who, with their greedy suckers, were to draw out the sickness from the body.

The opponents of this method spoke sarcastically of "vampirism," and maintained that more blood was being shed by Broussais' therapy than had been shed during the Revolution and the Napoleonic wars combined. In their irony they lagged far behind the truth. The hosts of leeches which Broussais had conjured up from the slimy depths of ponds and engaged against the human race, for sixteen years in succession, annually sucked 1,680,000 litres of blood from the French people.** If we add the loss of blood from ruthless blood-letting, we reach a figure which makes Broussais the bloodthirstiest man in world history, for at his instigation and on account of his error, twenty to thirty million litres of blood were shed in France alone.

—H. S. Glasscheib, M.D.: *The March of Medicine*, 1964.

*See Test Your Word Score Page 1659.

**A leech can imbibe up to seventeen grammes of blood. After three to four months it is sufficiently hungry to be used again, but it can serve only three times.

Derivatively Speaking

Pterygium—from Greek pterygion (wing)

*The Moving Finger writes; and, having writ,
Moves on: nor all your Piety nor Wit
Shall lure it back to cancel half a Line,
Nor all your Tears wash out a Word of it.*

—Omar Khayyam (?-1123)

Needle Biopsy of the Liver

A Five-Year Survey of the Menghini Technic

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NEEDLE PUNCTURE of the liver was first practiced in the late 1800's in diagnosis and treatment of hepatic abscesses. In 1939 Iversen and Roholm reported an aspiration biopsy modification as a diagnostic aid in acute hepatitis.¹ In recent years utilization of diagnostic needle biopsy has been limited because the most commonly used Vim Silverman needle requires skillful usage and produces significant morbidity even in the most experienced hands. In 1958 Menghini developed the "one-second liver biopsy" method utilizing a special thin wall, a small bore needle and a rapid aspiration technic.^{2,3} Even an inexperienced physician can apply the method with ease and with little fear of serious morbidity, by the simple expedient of reasonable caution.

The Menghini method was introduced at the Charles T. Miller Hospital by one of us (WRM) in 1961 without previous experience or demonstration. Since then it has been learned by staff physicians and by interns and residents on the service of Internal Medicine.

Method of Study

This paper presents an analysis of our experience with the Menghini needle technic during the five-year period 1962 to 1967. The clinical records of 59 patients subjected to 62 Menghini needle biopsies were studied with special attention to clinical-pathological correlations. The range of age among the 30 men and 29 women in the series was 24 to 85 years. Fifty-six biopsies were intercostal and six subcostal. Among the indications for liver biopsy were unexplained hepatomegaly, jaundice, abnormal liver function studies, suspected primary or metastatic tumor of the liver, or suspected systemic disease. Contraindications included prolongation of the prothrombin time five seconds or more above the control, and congestive hepatomegaly.

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Results

A summary of histologic diagnoses is shown in Table 1.

TABLE 1

Histologic Diagnoses of Menghini Liver Biopsy Specimens

Biopsy Diagnosis	No. of Biopsies
Normal liver	18
Nonspecific hepatitis	1
Cholangiolar hepatitis	1
Pericholangitis consistent with lupoid hepatitis	1
Laennec's cirrhosis	1
Portal cirrhosis	2
Postnecrotic cirrhosis	1
Biliary cirrhosis	1
Cirrhosis (unclassified)	5
Metastatic cancer	7
Fatty metamorphosis	11
Chronic passive congestion	1
Periportal fibrosis	1
Hemochromatosis	1
Hepatic abscess	1
Bile stasis	2
Insufficient tissue	7
	—
	62

Representative laboratory and physical findings in eighteen patients whose liver biopsy showed normal liver tissue are shown in Table 2.

TABLE 2

Results of Liver Function Tests and Physical Findings in the
18 Patients with Normal Tissue Diagnosis

	Total Tests	Abnormal Number	Percent Abnormal
Total serum bilirubin (above 1.1 mg.%)	15	1	6.7
Serum alkaline phosphatase (above 2.3 B.L. units)	12	6	50
Cephalin flocculation (+ 3 or above in 48 hrs.)	8	2	25
Thymol turbidity (above 4 units)	7	3	42.9
Bromsulfalein retention (above 5% in 45 min.)	11	8	72.7
	Number of Patients		Percent
Hepatomegaly	9		50
Splenomegaly	1		5.5
Ascites	2		11.1

Morbidity

There was no mortality and the two cases demonstrating objective morbidity had only a minimal asymptomatic pneumothorax after intercostal biopsy. Five patients had mild pleuritic pain; four had referred shoulder pain from trauma to the diaphragm; and seven complained of mild discomfort at the site of puncture.

All morbidity was transient and required only mild analgesia.

A summary of clinical-pathological correlations is shown in Table 3.

TABLE 3

Clinical-Pathological Correlation

	Number	Percent
Helpful in Diagnosis:	39	66.1
Confirmed the clinical diagnosis	19	32.2
Corrected the clinical diagnosis	20	33.9
Of No Help in Diagnosis:	20	33.9
Noncontributory	13	22
Inadequate specimen	7	11.9

The 12% incidence of inadequate specimens is partially explained by the fact that the operator in most of the cases was learning the procedure. Of the 13 biopsies which were non-contributory to the clinical diagnosis, four were actually misleading, since the normal liver tissue biopsy was followed by proven metastatic hepatic malignancy. In 20 cases (34%) the biopsy corrected incomplete or erroneous clinical diagnoses. Cases in this group included hemochromatosis, hepatic abscess, fatty metamorphosis, hepatic malignancy and normal liver.

Discussion

This study demonstrates the ease and value of the Menghini needle biopsy technic in inexperienced hands. The absence of severe morbidity and the 30% incidence of mild morbidity contrast with a reported mortality of about 0.1%^{4,5} and severe post-biopsy pain in 5 to 20%^{6,7} with other technics. In another study utilizing the Menghini method a 3.2% incidence of severe post-biopsy pain was reported.⁸

A demonstrated diagnostic value in 66% of cases in this series compares favorably with reports of other studies of this type.^{5,8,9,10,11} In seven of 11 cases of metastatic malignancy, the biopsy demonstrated the disease. Conn and Yerger report that needle biopsy will be diagnostic in 50% of all cases of metastatic malignancy of the liver, and positive diagnosis is increased to 90% when clinical signs of metastatic malignancy are present.¹²

It is well known that many cases with mild abnormalities in various liver function tests will have anatomically normal liver tissue by needle biopsy. This was well demonstrated in this series. None of these patients has shown

subsequent evidence of significant liver disease except the four cases with undetected metastatic malignancy.

Summary

The Menghini technic of needle biopsy of the liver was easily utilized by inexperienced physi-

cians as a valuable diagnostic tool. No mortality or severe morbidity occurred in 62 biopsies on 59 patients.

In two thirds of the cases the biopsy gave positive assistance in diagnosis. In one third the histologic diagnosis resulted in revision of the clinical diagnosis. We believe the method deserves more widespread application.

References

1. Iversen, P., and Roholm, K.: On Aspiration Biopsy of Liver, with Remarks on Its Diagnostic Significance. *Acta Med Scand* 102:1, 1939.
2. Menghini, G.: One-second Needle Biopsy of the Liver. *Gastroenterology* 35:190, 1958.
3. Menghini, G.: Two-operator Needle Biopsy of the Liver. *Amer J Dig Dis* 4:682, 1959.
4. Zamcheck, N., and Klausenstock, O.: Liver Biopsy: II. The Risk of Needle Biopsy. *New Engl J Med* 249:1062, 1953.
5. Vickers, F., and Price, D.: Liver Biopsy: A 10 Year Survey at Louisville General Hospital. *Kentucky Med Ass* 62:857, 1964.
6. Terry, R.: Needle Biopsy of the Liver with Special Reference to Modified Gillman Technique. *Brit Med J* 1:657, 1949.
7. Schiff, L.: *Diseases of the Liver*. Philadelphia, Lippincott, p. 161, 1956.
8. Parets, A., Schaffner, F., and Black, H.: Percutaneous Liver Biopsy with the Menghini Needle. *Amer J Dig Dis* 4:693, 1959.
9. Parker, J., Simon, M., Zimetbaum, M., Ackiron, L., Weingarten, B., and Allen, L.: Needle Liver Biopsy in Benign and Malignant Disease: Comparison of the Menghini and Vim-Silverman Technics. *Amer J Dig Dis* 7:687, 1962.
10. Gross, C., Millhon, W., Millhon, J., and Hoffman, D.: Liver Biopsy, a Report of Experience in 151 Cases. *Ohio Med J* 62:572, 1966.
11. Zamcheck, N., and Sidman, L.: Needle Biopsy of the Liver. I. Its Use in Clinical and Investigative Medicine. *New Engl J Med* 249:1020, 1953.
12. Conn, H., and Yerger, F.: A Re-evaluation of Needle Biopsy in the Diagnosis of Metastatic Cancer of the Liver. *Ann Intern Med* 59:53, 1963.

Mr. President—How Is Your Health* John Adams (1735-1826)

Our second President, John Adams, distinguished himself by reaching the venerable age of 90 years, eight months, and four days, a presidential feat unsurpassed before or since, even by Herbert Hoover, who would have had to live five months and 24 days longer than he did to exceed Adams' record.

Up to early middle age Adams was moderately well except for two chronic but not very disabling complaints: "eye weakness," uncorrectable by optometry at that time, and "nervousness," that indefinable but common affliction of sensitive intellectuals.

At age 35 Adams was assaulted by severe chest pain accompanied by chills and fever, the cause of which was not established but from which he recovered—not, however, without psychic trauma; for he ever thereafter regarded himself as a partial valetudinarian: a subsequent eye inflammation and palsied hand vindicating his gloomy conviction of his own infirmity.

When in Paris on official government assignment in 1783 Adams succumbed to an acute attack of influenza which so debilitated him that recovery took eight months. But it was not until he was in his eighties that the irreversible deterioration of old age caught up with him in much impaired vision and hearing, his arteriosclerotic decline thenceforth proceeding gradually and terminating in death from pneumonia on July 4, 1826: an eminent statesman's sad but appropriate commemoration of Independence Day.

*With acknowledgments to Karl C. Wold, M.D.

Pity costs nothing, and ain't worth nothing.—Josh Billings

Living Laboratory

A child had an acute case of xerophthalmia. The doctor found himself in an extremely difficult situation. He had to tell the little patient's mother that her boy, who had already lost his right eye, would inevitably lose the left eye as well.

The doctor was recording the results of his examination with a tarrying hand, putting off the moment when he would have to tell the mother the distressing truth.

But just as the doctor was about to break the terrible news of the boy's imminent blindness, a sudden idea crossed his mind. And what he said was not what he had initially intended to say.

"Bring him to our clinic at three today," he told her. "We'll see what we can do. But don't be late."

At three sharp the boy was hospitalized. A week later he was discharged. He walked down the street holding his mother's hand, and looked up at the shapes of passers-by, at the buses and houses about him.

His right eye was beyond repair. But the second eye was out of danger. It no longer looked lifeless. Its tissues had regained normal luster, and complete recovery was a certainty.

The doctor's sudden idea, which saved the boy from total blindness, hinged upon a blood transfusion, a rather unusual blood transfusion.

There is a class of substances whose presence in man's diet is absolutely essential. They are called vitamins. One of them is vitamin A. It occurs in animal fats, and is particularly plentiful in cod liver oil. But what is most important to us at this point, vitamin A cures xerophthalmia. But at that time vitamin A was not as yet being produced in a form that could be injected into the blood, or subcutaneously.

The doctor's sudden idea boiled down to a method of supplying the child's organism with the required amount of vitamin A. Two hours before the transfusion the donor was made to drink a whole glass of cod liver oil.

At the moment of the transfusion the donor's blood was saturated with vitamin A, absorbed from the intestines. A test made beforehand at the laboratory confirmed this. Along with the transfused blood the boy's body thus received a dose of vitamin A which proved big enough to terminate the xerophthalmic process. It saved the child's eye.*

*L. Fridland, M.D.: *The Achievement of Soviet Medicine*, 1961, edited and translated from the Russian by W. Horsley Gantt, M.D.

Remedies for Jaundice

For the cure of jaundice, the ashes of a stag's antlers are employed; or the blood of an ass's foal, taken in wine. The first dung, too, that has been voided by the foal after its birth, taken in wine, in pieces the size of a bean, will effect a cure by the end of three days. The dung of a new-born colt is possessed of a similar efficacy.

—Pliny

There are three kinds of people in the world: the wills, the won'ts and the can'ts. The first accomplish everything; the second oppose everything; the third fail in everything.

—Eclectic Magazine

The Brain

Some Psychobiologic Groundrules for the Lifegame

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IT IS A BASIC principle of logic that every functioning system has its own set of "ground-rules" which allow it to continue functioning. Whether the system we are talking about is a social organization, a steam engine, or a living animal, there are going to be certain basic consistencies in their functioning. Each system will have an energy source to activate it, an arena or field in which to function, and control mechanisms to limit activity.

Governor Mechanism

The brain has basic and fundamental rules which describe the way it regulates the biologic energy which activates it. It has multiple control systems which stimulate and inhibit the function of interconnected areas. These impulses then blend and fuse into coordinated behavior.

In order to explore the fundamental rules which are functioning in the brain, it will be necessary to first describe some of the negative and positive limbs of feed-back circuits in a simple machine like the steam engine. The energy input which drives this machine is heat, which raises the steam pressure of the boiler and activates the piston to accelerate the drive wheels. When these wheels reach a pre-determined speed, they will activate a governor which will decrease the energy input, so that the machine will not exceed its critical limit. Likewise, the influence of positive and negative feed-back factors is a matter of primary importance in understanding the effect which the basic brain systems have on each other.

The Human Brain

The human brain can be described as containing three brain systems which are superimposed, one upon another. Paul MacLean has described these as the reptile brain, the early mammal brain and the primate brain (late mammal).¹

The Reptile Brain

The area which he describes as the reptile brain is the brain stem, and contains the motor nuclei of the cranial nerves, and the reticular activating system which determines the activity of the sleeping-waking cycles and the primitive basis of "consciousness." Centers here regulate blood pressure, heart rate, digestion, and even the movement of the eyes. Some rather simple or primitive aspects of sexuality, such as penile erection, are represented here, along with nuclei which are parts of circuits dealing with balance and equilibrium. The motor cells of the primate brain stem are principally activated and controlled by influences which descend upon it from higher areas which developed later in the course of evolution. The metabolic activity of the reptile brain is more primitive than that of the early mammal brain. Both of these brain systems have a lower uptake and utilization of oxygen and carbohydrate than the primate brain.² We would naturally expect that the enzyme systems which regulate metabolism will be different in the reptile and the mammal brain, since the reptile brain will still function at temperatures which are much below those which the mammal brain must have for optimal function. It is useful to recognize this primitive metabolic potential of the brain stem, because it helps us to understand why it can still function when other areas of the brain have been inhibited and the patient has become comatose.

Early Mammalian Brain

The second system is the early mammal brain, also called the Limbic System, which includes two rather complicated pathways connecting the hypothalamus with the temporal lobe nuclei. It contains the structures which were previously called "the rhinencephalon", or literally the nose brain. These are circuits which connect the olfactory nerve* with areas which are related to feeding, fear, and sexual arousal. The glucoreceptor mechanism is situated in the center of the hypothalamus and has a very important effect on nearby nuclei. These happen to include some which are involved in the activities associated with the sense of smell in early mammals.

Late Mammalian Brain

These circuits have remained during the course of evolution, and by the time the primate brain has evolved, they have become circuits involved with emotional experience. The glucoreceptor mechanism is located principally in the ventromedial nucleus of the hypothalamus and is activated by elevation of the blood sugar to inhibit the activity of the nearby feeding mechanism in the lateral hypothalamus.³ When this occurs, the animal stops feeding: a remarkably clear illustration of the negative feed-back limb of a complicated circuit. This circuit involves activation of the feeding drive as the glucoreceptor mechanism becomes inactive because of food deprivation and initiates behavior which results in eating. This will elevate the blood sugar and activate the glucoreceptor mechanism. When it is activated, it acts in a manner similar to the governor of a steam engine and reduces the energy input into the system through the inhibition of the feeding drive, thus initiating a period of food deprivation and the start of another cycle.

Drive Behavior

This gives us an opportunity to define the meaning of "drive behavior" in psychiatry.

Drive Satisfaction

It is behavior which results in a change of the input into the central nervous system, so that a negative feed-back circuit is activated and an excited area of these emotion circuits inhibited. The process of activation of the negative feed-back mechanism is called "drive satisfaction."

Waking Center

The posterior hypothalamic area is also and simultaneously a part of the reticular activation system of the brainstem and contains a waking center.⁴ The feeding behavior of infants reveals the influence of the glucoreceptor mechanism on the waking center. When the ventromedial nucleus is activated by elevations of blood sugar following feeding, it sends out inhibitory impulses to the posterior hypothalamus and inhibits the "waking center", causing the infant to fall asleep. As the infant brain matures to

*See Test Your Word Score Page 1659.

childhood, more influences begin to affect the posterior hypothalamus, and it is not so regulated by the influence of the blood sugar on the ventromedial nucleus. The influence can still be found in the "siesta effect" which a heavy meal has, even on adults. *In order to evade the sedative effect of eating, it is necessary to increase the sensory input into the reticular activation system with physical activity in order to keep the posterior hypothalamus aroused.*

The Anterior Hypothalamus

The anterior area of the hypothalamus is oriented toward the activities of the parasympathetic division of the autonomic nervous system. Stimulation here with depth electrodes will activate the mucosa of the stomach and increase the production of gastric acids when the vagus nerve is intact. This is associated with the development of peptic ulcers.⁵ When the disease of diabetes occurs, it causes a chronic elevation of the blood sugar which activates the ventromedial nucleus. If the relationship exists with the anterior hypothalamic area which we have found with the lateral and posterior areas, we would expect that diabetes should protect against peptic ulcers. In fact, it does. The rate of peptic ulcers in the normal population is four to five times as high as the diabetic population.^{6,7}

The various circuits within the limbic system have been described differently by different observers, but they do basically agree that there is a circuit which connects the anterior hypothalamus with the amygdala, and another which links the posterior hypothalamus with the hippocampus. MacLean has designated these as circuits associated with self-preservation and species preservation.⁸

The Primate Brain

The third system of the human brain which we can focus on has been called the primate brain consisting of the neocortex and the thalamocortical circuits which connect it with the lower two systems. Its influence on these lower centers, particularly the posterior hypothalamus which is part of the reticular activation system, is to provide an inhibitory control of impulsive and aggressive behavior. This

is why decortication of animals is associated with the development of "sham rage."^{*} These animals are constantly on the verge of aggression and are very likely to attack anyone who increases the sensory input into the reticular activation system. Direct electric stimulation of the posterior hypothalamus can also elicit "sham rage" and cause changes in blood sugar identical to those caused by the emotion of fright or anger.⁹

Disturbed Cortico-Thalamic Circuit

This factor is of great importance in understanding the inappropriate and impulsive rage behavior of senile elderly patients. The basis of their consistently being on the verge of "sham rage" can be found in the loss of physiologic activity of the cortico-thalamic circuits associated with cortical atrophy. The cortex of the brain, the last portion to evolve and the last to become myelinated and then mature, is the most sensitive to the biologic stress of aging. While the more hardy and simple metabolic activity of the brain stem continues to function, the cortex is subject to physiologic inhibition and eventual atrophy.

The activation of the sympathetic functions of the posterior hypothalamus will be influenced by the cortico-thalamic circuits, which influence the reticular system, and circuits of the limbic system, particularly one which connects the amygdaloid nucleus of the temporal lobe with the ventromedial nucleus of the hypothalamus. The ventromedial nucleus is an intrinsic part of the glucoreceptor mechanism and has a distinct inhibitory effect on the posterior hypothalamus. The smoothly integrated functions of these circuits associated with both the limbic system of the early mammal brain and the primate brain are required to permit appropriate goal-directed behavior.¹⁰

Chronic Brain Syndrome

It is this event which can allow us to understand the paradoxical response of the senile, and many of those with chronic brain syndrome, to the barbiturates, which act to sedate the neocortex of the brain as well as the reticular system. When this occurs in an elderly person on the verge of "sham rage," he is frequently "stimulated" into impulsive, confused, and usually angry behavior.

^{*}See Test Your Word Score Page 1659.

Behavior Pattern

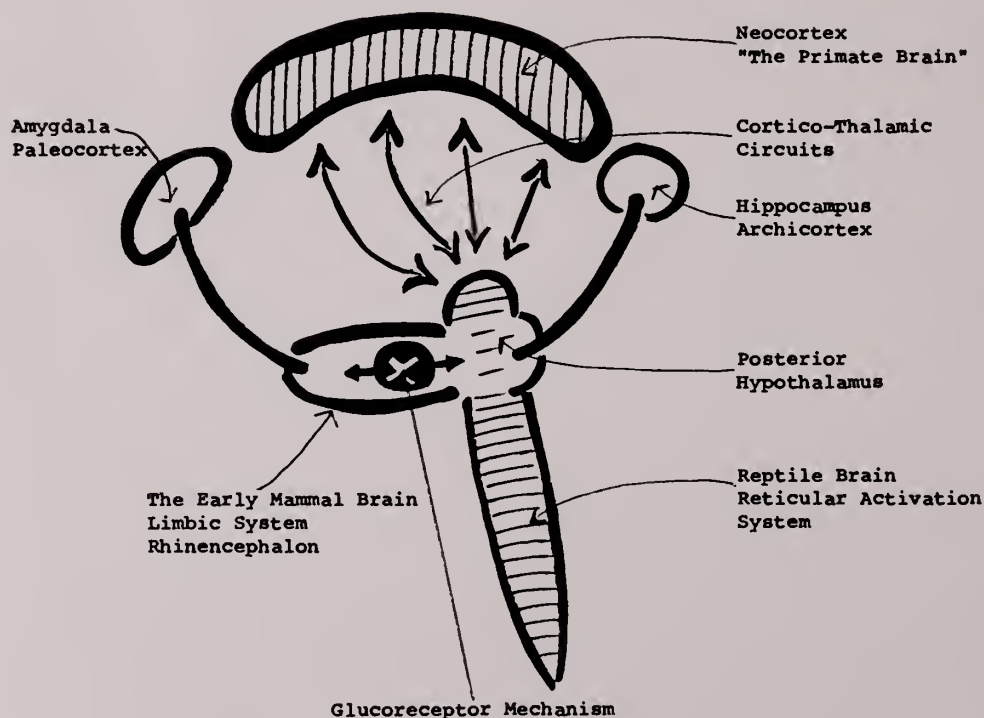
The recognition of these basic groundrules for the experience of life can be of considerable help in understanding more about basic patterns of behavior.

Love and Contentment

The effect of the glucoreceptor mechanism provides us with some neurophysiologic insight into the oral phase of infancy. Psychoanalytic theory has emphasized the significance of feeding and sucking as reassurance of love and expectation of contentment. Successful experiences at this stage of development have been said to be basic to the development of trust. These theories can be placed in a much better physiologic perspective when the influence of the glucoreceptor mechanism of the ventromedial nucleus of the hypothalamus is considered: the circuit which is activated by the elevation of blood sugar resulting from the oral feeding activity. This event will inhibit

both the activity of the feeding area of the lateral hypothalamus and also the activity of the posterior hypothalamus, an area principally associated with the activities of the sympathetic division of the autonomic nervous system. Activation of this area has been shown to cause "sham rage" behavior.⁹

When we recall that the newborn infant is basically a "brain stem preparation" actually functioning in a state similar to decortication, we can begin to understand his action and emotion when hungry. The glucoreceptor mechanism is unable to function following food deprivation. This reduces its capacity to inhibit surrounding areas and they are released to express the primary activity which occurs on stimulation. The state of food deprivation then releases the posterior hypothalamus and the "waking center" is activated, awakening the infant. Stimulation of this area can be associated not only with "sham rage" but also with hyperactivity, destructive behavior, anxiety, or fear. This is why the infant appears to be so angry when he cries.



Figure

The three basic brain systems which fuse and blend in the adult brain to permit coordinated, goal-directed behavior.

The anger is an inevitable part of the activation of the hypothalamus which is a part of his feeding cycle. The act of sucking will become a part of a conditioned response in which relief from emotional distress will soon follow.

Feeding and Relief from Anxiety

To a certain extent, we can find a neurophysiologic basis or background for some theories about early infancy. Feeding is associated with relief from anxiety. But to the extent that this observation is valid, it simultaneously invalidates any neurophysiologic importance to the concept of "anality." Sucking and feeding will elevate the blood sugar and have some profound effects on the emotional circuits of the rhinencephalon of the limbic system. Defecation cannot have such an effect. A bowel movement may occur after stimulation in some areas of the brain, but this action has more similarity to the movements of the hand in Jacksonian epilepsy than it does to an important emotional event, such as activation of the glucoreceptor mechanism.

Maturation of the Brain

As we consider the gradual development of the child's brain, we find that at the age of four it has finally achieved about 90% of the weight it will have as an adult brain.¹¹ This is the approximate period of time that the child is learning to control his aggressive behavior. He is now learning to accept and identify with rules. It has been found that while activation of the posterior hypothalamus can cause aggressive behavior, this is associated with the medial area. The lateral area of the posterior hypothalamus is excited by testosterone, and activation of it is associated with sexual arousal and orgasm.¹²

This, then, provides us with an organic, neurophysiologic explanation for the development of sexual guilt. As the child learns

rules of behavior and safe limits are set for him to grow in, he must learn to inhibit his aggressive impulsiveness. The continuing maturation of his cortex is finally providing him at four or five years of age with a psychobiologic mechanism which can control and inhibit the posterior hypothalamus. It can be proposed that this inhibitory process physiologically *includes both the medial and the lateral hypothalamus*. The child then will develop a sense of guilt about sexual arousal or curiosity which will be comparable to his guilt about aggressive or "bad" behavior. He need not ever have been threatened or punished for any sexual actions. He will develop a sense of sexual guilt because the inhibitory influences of the cortex have been placed on the entire posterior hypothalamic area. It is of interest that the Rorschach responses of children also change during this time, and some of the impulsiveness of earlier records is now shadowed by doubt. This is the phase of development that Freud identified as the Oedipus conflict.

To the extent that this is correct, it can help us to understand the universality of an almost compulsive need to masturbate during male adolescence. This could be the mechanism by which the blanket inhibition of the area during childhood is altered, so that sexual arousal can be integrated into a guilt-free area of personal behavior.

Conclusions

This review of three identifiable systems in the brain provides us with some psychobiologic ground rules to use when we consider the meaning of different factors which influence behavior. To recognize the location and connection of various circuits can help us to better understand and predict behavior and symptoms. It can also help us to recognize factors which we might want to augment or diminish in order to change behavior and relieve symptoms.

References

1. MacLean, P. D.: Further Studies on Cerebral Representation of Penile Erection. *J Neurophysiol* 26:273, 1963.
2. Himwich, H. F. and Fazekas, J. F.: Comparative Studies of Metabolism of the Brain of Infant and Adult Dogs. *Amer J Physiol* 132:454, 1941.
3. Anand, B. K.: Nervous Regulation of Food Intake. *Physiologic Review* 41:677, 1961.
4. Ranson, S. W.: Somnolence Caused by Hypothalamic Lesions in the Monkey. *Arch Neurol Psychiat* 41:1, 1939.
5. Pearl, J. M., Richie, W. P., Gilsdorf, R. P., Delany, J. P., and Arnold, L.: Hypothalamic Stimulation and Feline Gastric Mucosal Cellular Population; Factors in the Etiology of Peptic Ulcers. *JAMA* 195:281, 1966.

6-12 May be secured from the author or the reprints.

A Wharf Rat

We could never tell where ambulance calls would take us, but one thing we knew—there would be a policeman waiting at the other end of the telephone, for all the calls were sent in by the police.

One brilliant day in early spring with a sting of frost still in the air, a call took me down to the docks and onto a big sailing vessel anchored there. While rigging up their sails that morning the sailors had come upon the crushed body of a little boy possibly eight years old, high up, hidden in the folds of one of the biggest sails. There was no doubt that he was dead, and that freezing had overtaken him up aloft in the sails. Was his death due to an accident or murder? Did anyone know the boy? What was his name? The police scouted the theory that it could be foul play. An old stevedore came along and stopped to see what the excitement around the ambulance was all about; he edged in to the little group and when the policeman asked, "Can anyone identify the boy?" he said, "Sure, I know that kid—he's a little wharf rat."

"Do you know where he lives?"

"Sure, he lives along the docks here hiking from slip to slip."

"Do you know his name?" the policeman persisted.

"He aint got no name that I know of, but we all give him a break when we got it, with grub and clothes."

This laconic information seemed to satisfy the police, who figured that he had climbed up into the folds of the big sail for a night's rest and during the night the wind had changed and the big boom had shifted its position, crushing the little boy to death in his sleep. No one seemed surprised or concerned, for he was just a little wharf rat.*

*Emily Barringer, M.D.: Memoirs of a Lady Ambulance Surgeon. Bowery to Bellevue, 1950.

(President's Letter continued from page 1613.)

to the Editor", or some such response to my discourse. What I have said about our own Medical School could be said about most other schools in this country, I am sure.

I should like to take advantage of this space to say a great "Thank you" to Dick Magraw for what he has started here at the University of Minnesota. We wish him well in his new endeavor, and are pleased that he will be in a policy-making position, where his type of attitude is sorely needed. I am confident that he will not lose the excellent perspective which

he now has, even though he moves up to the Federal level. He will make his voice heard, in his own quiet, persistent way.



C. G. Sheppard, M.D.

President

Minnesota State Medical Association

It is easier to fight for one's principles than to live up to them.

—Alfred Adler

God gave us our memories so that we might have roses in December.

—James Barrie

Here's to woman! Would that we could fall into her arms without falling into her hands.

—Ambrose Bierce

Traumatic Brain Syndrome

Psychological Sequelae in a Case Undergoing Remission

WILLIAM T. LUCKEY, M.D.
Minneapolis, Minnesota

A FEW YEARS AGO a patient's wife told a social worker who was making a home visit: "I feel my intentions have been misinterpreted by your clinic. I was told that he would never get along outside the hospital and that it might be better if I tried to forget him. It is not true that I don't want him to come home; I simply feel that if he does, there will be many adjustments to make by all of us."

Her husband was leaving the hospital (a chronic psychiatric institution) for the first time since a near fatal accident, which had occurred in 1960; he had been continually hospitalized for a period of four years. His diagnosis was that of chronic brain syndrome due to head trauma.

This particular case is important for two reasons: first, it demonstrates the difficult social and intrapersonal problems that may face a patient who was once considered hopelessly disabled but who is now slowly recovering. Second, it reminds one again of an old clinical axiom which one of my neurology instructors used to repeat over and over: "Don't ever give up hope for some latent recovery in even the most severe head trauma—and be ready for some surprises."

Case Report

This 46-year-old white male was involved in an aircraft accident in 1960 while on active military duty. At that time, according to his service records, he suffered severe head trauma and was in a comatose state for about one month after the accident. After regaining consciousness, he had grand-mal seizures which had to be controlled eventually with Dilantin. After the first year it was felt that he had "stabilized;" however, he was considered markedly impaired mentally and emotionally.

Personality Changes

Gross personality changes included frequent mood swings and uncontrolled hyperactivity; severe memory loss, disorientation, and impaired judgment were present on repeated mental status examinations. At this point his wife was told that his chances for ever living outside the hospital were slim and that it might be best if she began to rearrange her life accordingly.

Family Status

The patient was the second of four siblings (having three sisters); there was no history of mental problems in his family or his wife's family. He had graduated from high school and planned a career in the service. He had four children and no history of marital problems; neither he nor his wife had needed psychiatric help prior to his accident. Both he and his wife considered their marriage successful. The patient, at the time of his accident, was working in a supervisory capacity, directing 50 or more men in his department.

Since his hospitalization at a mental institution, the wife had started seeing another man. She lived in a modern, roomy, middle-class home, paid for by the patient's service compensation; the patient used about thirty dollars of this each month at the hospital. She had remained on good terms with her mother-in-law, but not with other family members on the patient's side. One of his sisters felt strongly that the present situation was regarded favorably by the wife and that she did not actually want her husband released. She had not been adept at handling finances and she had been forced to borrow money over the preceding few years to meet expenses.

The patient was released to a foster home after four years of hospitalization. Although still showing marked memory deficit and personality change, his mental condition had "improved." He spent the next few months in a Veteran's Day Treatment Center; during this time he did not work or take part in activities. His attendance rapidly became sporadic and his case was closed after six months; it was later discovered that he had moved to another state and had held a job for about a year before returning to this area.

Clinical Improvement

Upon returning, he again contacted our outpatient clinic. There now seemed to be a marked improvement in his condition; he was less impulsive, more active socially, and much of his memory deficit had cleared. This clinical improvement was verified by comparison of his present psychological test results (1966) with those in 1964 (his first period of treatment at our clinic). The two Minnesota Multiphasic Personality Inventory profiles were of the same basic type (1348), but the current one was entirely within normal limits. In 1964 he had an age-corrected Shipley-Hartford I.Q. of 108 (a verbal raw score of 34 and an abstraction raw score of 18); now his total Shipley-Hartford I.Q. was 125 with a 34 verbal raw score and a 30 abstraction raw score. A Wechsler Adult Intelligence Scale was also administered and showed a full-scale I.Q. of 126; this again verified the marked improvement since 1964 (primarily due to higher performance, as the verbal score had remained the same).

The patient acknowledged that he was "feeling better;" however, he saw himself as "permanently disabled." He was now planning to accept life-long unemployment; he spoke of wanting to work, but he

could foresee only failure if he tried. When reference was made to his improvement, he attempted to *emphasize* the residual problems with his memory and judgment; in short, he saw himself as chronically ill and seemed to resent being pushed back into a "normal life." Several staff members jointly agreed that psychological factors (his poor self-image, his fear of failure) were now more inhibiting than his residual cerebral dysfunction. For the first time, he began to resort to somatic concern when faced with task responsibility at the day treatment center.

His wife still stated that she would take him back into the home if his improvement continued; our impression was that she feared negative reaction by the patient's family and the clinic, and would probably accept any good reason to delay this return. The patient wanted to return and spoke of increasing his contact with the family. He felt, however, that the greatest roadblock to his being received back into the family was their acceptance of his "irreversible problem." He was asking his wife and children to consider him an "invalid."

Psychiatric and Social Implications

This case demonstrates three important psychiatric variables in chronic head trauma cases:

Improvement

Organic brain syndromes can undergo considerable improvement. In cases of trauma, especially in patients with good pre-morbid history, the possibility of latent recovery should be considered in advising relatives.

Marital Adjustment

The spouse of such a patient must (at least temporarily) build a new life; how he or she plans their future may depend upon what the physician says about the possibility of recovery. In this case, therapists at our clinic disagreed over the wife's adjustment and basic motivation. Some felt that *latent* marital conflict was at the root of her attitude and behavior toward the patient, while others saw her adjustment as a reasonable means of survival for a woman faced with such a problem. It was generally agreed that she had at first resigned herself to the idea that her husband would always remain in the hospital.

Psychological Survival

Traumatic encephalopathy may impose distinct psychological problems upon a previously stable personality; these psychological prob-

lems may not be solved when the encephalopathy improves or disappears. With recovery the patient's self-image seems particularly vulnerable; he may begin to show a fear of failure in attempting even minor tasks and speak of himself as a totally "different" person. Minor disabilities may be utilized to avoid responsibility once readily assumed. If in constant association with other chronically ill patients (of various etiologies) during his recovery phase, he may learn new symptoms, such as somatic concern. If such a patient once gives up on himself and tends to adapt his goals to those of a dependent, unemployable person, he may even fight to maintain what to him seems the safest means of survival.

Comment

Such a case forces the therapist to make value decisions which influence the lives of the patient, his spouse, and his children. Although there will probably never be any set formula for handling such a human crisis, this case and others have shown me that there may be some guidelines for the clinician to follow.

Repeated, early evaluations of the neurological and psychological deficit are important for both the physician and the family. There is, in my opinion, a definite psychological lift when a spouse knows that a hurried decision about a bad prognosis has not been made.

Of course, one cannot guarantee a family that improvement will occur. But it seems best to suggest that the spouse wait for a period of two or three years before planning a life independent of the patient. I suggest that the physician ask the spouse to wait out this time for a final evaluation (and prognosis).

If the spouse refuses to wait, this can probably be accepted as a rough test of motivation. Under these circumstances, one should probably plan initially to create for the severely injured patient a new life outside his family, since eventual improvement by the patient would be unlikely (by my experience) to influence the spouse's original decision.

If the spouse voluntarily waits, I feel that some psychological help should be given by hospital or outside medical personnel. The spouse should be well aware that total recovery is unlikely to occur, and that the interpersonal

relationship will probably never be the same as before.

With evident improvement the family must still be allowed to make their own decision about taking the patient back into the home. At the end of the waiting period, all aspects of the neurological and mental status should be discussed with the family. If possible, they should accept the patient for several trial periods at home. If they appear able and willing to cooperate, family counseling should be instituted (including the patient).

If the family is unwilling to accept the patient, I do not feel that either professional or social pressure should be used on the family. I have never seen this help either the patient or the family. It has served only to decrease the precarious self-esteem of the patient. Let the relatives make their own decision based on an honest medical evaluation; it is far better to gear the patient for a life independent of the family if he is not truly welcome back.

Most physicians do not like to make such value decisions; however, in chronic traumatic cases this may lead to great interpersonal suffering for a patient's spouse and children. If the patient *does not improve*, I would encourage eventual separation; guilt feelings on the part of the wife should not be allowed to influence her decision. When there are children, a severely disabled patient may be an indifferent or actually cruel parent; and he may often act in a parasitic fashion toward the spouse. After seeing several examples at first hand, I feel that one is obligated to consider and render judgment on whether a spouse should accept a permanently disabled patient back into the family. If need be, psychotherapy sessions should be recommended for the spouse and children with the goal of complete separation from a severely brain-damaged patient.

For a husband and wife who have been married for some time, I do not feel that waiting for several years is an unreasonable request by the physician. Such a sacrifice of time by the spouse is only humane; it also may prevent rash and on-the-rebound behavior. I also feel just as strongly about blindly forcing a spouse and children to accept a severely disabled patient back into their home; for the sake of the children, it may be the duty of the physician to work for a permanent separation.

Medical Quackery

"PHYSICIANS, AS conservators of the public health, are bound to bear emphatic testimony against quackery in all its forms."

Is this a quote from proceedings of the American Medical Association's Clinical Convention in Philadelphia?

The meeting was in Philadelphia, but the year was 1847!

So you see, from its very inception 118 years ago, the American Medical Association has been battling quackery and it is dedicated to a continuation of this warfare against wasting the nation's health and its health care dollar . . . of fighting fraud at the bedside of ill and desperate people.

For, as long as there are human beings, there will be human nature . . . and quacks—pretenders to ability they don't possess—to take advantage of the fact.

The health quack is not so easy to spot these days. The stovepipe hat and the pitchman's hawking have gone. In their place are their space-age counterparts, the suave apparently-sophisticated super salesmen with the Madison Avenue manners.

These merchants of menace, more insidious and unscrupulous than ever, have many new products, worthless diet fads, worthless food supplements, worthless cosmetic devices and treatments, worthless "cures" for everything—even into the area of brain-damaged children and other mental illness.

They bilk the undiscerning—the uninformed, the desperate, the unsuspecting of all ages—of

millions of dollars a year. The estimates of the costs of medical quackery are at best calculated guesses, but they have gone as high as a billion dollars a year. And one authority in the field of quack-fighting has stated that "medical quackery each year costs more lives than all crimes in the United States."

It is the cost of life—and health—that has placed America's physicians in the front lines of the war on quacks. It is the insidious side effect of quackery with which medicine concerns itself—the delay in proper medical care that may cost life itself.

It is for this reason, too, that the medical profession is dedicated to education of the people about cultism.

The House of Delegates of the American Medical Association said in 1933: "Either the theories and practices of scientific medicine are right or those of the cultists are right and those of scientific medicine are wrong, or the theories and practices of the cultists are wrong." And in 1961, it said: "There can never be a majority party and a minority party in any science . . ."

After the quack or the cultist has extracted his pound of flesh—after the damage is done and after the sick may have become the dying because of the delay in proper care—scientific medicine usually is called upon to pick up the pieces.

Medicine has tried and will continue to try to do that job, too, but how much easier the job would have been—how many lives would have been saved—if . . .

American Medical Association

Medical Men on Postage Stamps

Theodor Billroth (1829-1894), Austrian surgeon, is regarded as the founder of modern abdominal surgery, having performed many successful intestinal resections and enterorrhaphies during his career. In 1872 he made his first resection of the esophagus, in 1873 his first complete excision of the larynx, and in 1881 his first resection of the pylorus. Also performed by him in 1891 was the first recorded interilio-abdominal amputation. In recognition of his phenomenal achievements Austria issued a postage stamp in his honor in 1937.

Robert Picque (1877-1927) was a French army general and military surgeon in World War I, whose pioneer work in surgery at the front was commemorated by France in 1951 on a postage stamp issued in honor of Military Medicine. Along with Picque, portraits of Colonels *Roussin* and *Villemin* also appear on the stamp.

BREAK IN INFORMATION
PUBLISHED SEP 68



Editorials

Brucellosis Re-Examined

WHEN SIR DAVID BRUCE concluded his lecture on "The Extinction of Malta Fever" in 1908 he said, "With this chart, which shows the practical extinction of Malta fever, my discourse comes to a close." However, as the Mayo Clinic group points out in a timely review in the October issue* brucellosis is still a perplexing clinical problem.

The clinician must bear in mind that brucellosis is not basically a human disease but a disease of animals transmissible to man. Wherever the disease continues to exist in animals human illness will result. Although the animal brucellosis eradication program in Minnesota has reduced the incidence of the disease remarkably there still exists a reservoir of potential human illness in infected cattle and swine. Brucellosis was detected a short time ago in a flock of sheep in this state.

While human brucellosis appears most often as the sporadic acute or chronic case, epidemics of human cases still occur, mostly due to *Br. suis* and of swine origin. As an example, from June 1966 to May 1967, 43 cases of brucellosis were detected in a meat packing plant in the state of Virginia. Epidemiologic studies on swine introduced into the plant revealed that up to 58 per cent of sows were infected!

In the United States human brucellosis is rarely encountered following the ingestion of dairy products, largely because of the widespread practice of pasteurizing milk. The dis-

ease is primarily an occupational illness occurring in packing plant employees, livestock producers and veterinarians. We have been encountering more and more veterinarians who have accidentally inoculated themselves with the vaccine, *Br. abortus* 19, while immunizing cattle. Because most of these persons had been infected previously with brucellae they had acquired hypersensitivity, and the introduction of organisms resulted in localized inflammation and systemic reactions of chills and fever. Apart from an occasional localized tissue necrosis these individuals recover in a short period with and without antibiotic therapy.

The diagnosis of brucellosis should be suspected in any individual with an ill-defined febrile disease, whose occupation brings him into direct contact with cattle and swine. Sheep constitute a minor problem in the United States. Unexplained lymphocytosis in such patients is a helpful diagnostic aid. The most helpful diagnostic procedure is the brucella agglutination test. Rarely do either acute or chronic cases occur without demonstrable agglutinins. In the World Health Organization Brucellosis Research Laboratory at the University of Minnesota Medical Center the clinical significance of brucella-agglutinating antibodies has been further defined by detecting 7S agglutinating antibodies only in serum from patients with active disease. Furthermore, in contrast with 19S brucella antibody, which is also present, only 7S fixes complement, so that we have found the brucella complement-fixation test highly reliable for detecting evidence of active disease, particularly in the more

*MacDonald, Giles F., Kelly, Patrick J. and Martin, William J.: Paradox of Brucellosis—Decreased Incidence but Increased Difficulty in Clinical Recognition. Minnesota Med 50:1469, 1967.

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chronic cases and in those with a low titer of agglutinins.

Tetracycline therapy alone is adequate for the majority of cases of brucellosis. The dose is 0.5 Gm. by mouth four times daily for 21 days. In the more severe cases, especially those with suppuration due to *Br. suis*, simultaneous therapy with streptomycin is carried out; 1.0 Gm., intramuscularly once daily for 14 days. For severe and toxic states corticosteroid therapy is advised for three to four days

along with antibiotic treatment. Prednisone in dose of 20 mg. twice daily may be given by mouth.

Two WHO publications are advised for those seeking concise and authoritative statements on the various phases of brucellosis that will appeal to clinicians, laboratory workers and public health personnel. They are: "Laboratory Techniques in Brucellosis" by G. G. Alton and L. M. Jones, WHO Monograph Series No. 55, 1967, Geneva, and "Joint FAO/WHO Expert Committee on Brucellosis", Fourth Report, WHO Technical Report Series No. 289, 1964, Geneva.

*Regents' Professor of Medicine, Director, WHO Brucellosis Research Laboratory, University of Minnesota Medical Center.

Wesley W. Spink, M.D.*
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Solitary Myeloma (Solitary Plasmacytoma) of Bone*

The relationship of solitary plasmacytoma to multiple myeloma has remained controversial despite many publications. Even the existence of solitary plasmacytoma has not been accepted by all students of the subject.

Solitary plasmacytoma is more frequent in males than females and involves all age groups, with the greatest incidence in the sixth decade of life. Pain often heralds the clinical onset of the disease. It can appear as a swelling which may or may not be painful. The bones most frequently involved by solitary plasmacytoma are the vertebral bodies. Next most frequently involved are the pelvis, femur, and humerus. Pathologic fractures are not uncommon, and paraplegia may occur.

The roentgenographic picture may closely resemble that of a giant cell tumor of bone or a large osteolytic lesion.¹ The former consists of a sharply demarcated osteolytic multicystic area. The area of destruction may be covered by trabeculae. It should be noted that some of the lesions of widespread multiple myeloma may have a cystic trabeculated appearance indistinguishable from that of a solitary plasmacytoma. The cortex is usually intact and no periosteal reaction is seen. The osteolytic type presents a sharp margin. No proliferative bony changes or trabeculae are seen. It is more

commonly found in the spine, and a paravertebral soft-tissue mass may be visible.

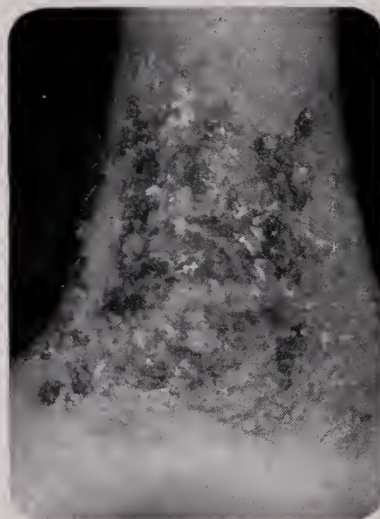
The diagnosis rests on histologic proof of a tumor consisting of plasma cells. It should be emphasized that it is impossible to separate solitary plasmacytoma of bone from multiple myeloma histologically.

In addition to histologic proof of a lesion, complete skeletal roentgenograms must show no other lesions of myeloma. It is essential that bone-marrow aspiration show no evidence of multiple myeloma. This examination may reveal increased numbers of plasma cells long before other manifestations of disseminated disease appear. Electrophoresis of the serum should show no "myeloma spike." Rare exceptions to this can occur; an example is Lane's² patient who had a plasmacytoma of the jaw. There was a small peak of gamma mobility which disappeared several months after the tumor was removed. Homogeneous M peaks in the urine on electrophoresis and Bence Jones proteinuria ought to be absent. Although Bence Jones proteinuria has been reported in solitary plasmacytoma, its occurrence strongly suggests multiple myeloma. The presence of anemia, hypercalcemia, increased sedimentation rate, and azotemia suggests multiple myeloma rather than a solitary lesion.

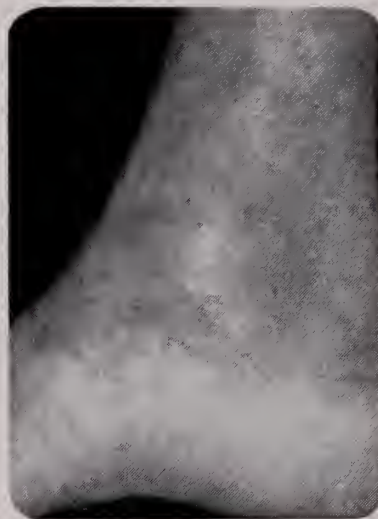
The most controversial criterion for the diagnosis of solitary plasmacytoma of bone is the length of follow-up necessary before one

*Ramos, P., Johnson, P. L., and Kling, R. R.: Solitary Myeloma of Bone: Report of a Case 13 Years after Diagnosis. *Minnesota Med.* 50:1073, 1967.

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effects are encountered, the drug should be discontinued and appropriate measures taken. Use on infected areas should be attended with caution and observation, bearing in mind the potential spreading of infection and the advisability of discontinuing therapy and/or initiating antibacterial measures. Generalized dermatological conditions may require systemic corticosteroid therapy. Steroid therapy, although responsible for remissions of dermatoses, especially of allergic origin cannot be expected to prevent recurrence. The use over extensive body areas, with or without occlusive nonpermeable dressings, may result in systemic absorption. Appropriate precautions should be taken. When occlusive nonpermeable dressings are used, miliaria, folliculitis and pyoderma will sometimes develop. Localized atrophy and striae have been reported with the use of steroids by the occlusive technique. When occlusive nonpermeable dressings are used, the physician should be aware of the hazards of suffocation and flammability. The safety of use on pregnant patients has not been firmly established. Thus, do not use in large amounts or for long periods of time on pregnant patients.

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can be assured that dissemination will not occur. Christopherson and Miller³ used a three-year period without evidence of dissemination for the diagnosis of solitary plasmacytoma, while Pasternack and Waugh⁴ followed their patients from four to 10 years. However, dissemination or recurrence of plasmacytoma has occurred at nine to 12 years,^{5,6} and one case as late as 21 years⁷ after the initial lesion had been found. Thus one's diagnosis of solitary plasmacytoma is not safe for many years. Even the interesting patient described by Ramos, Johnson, and Kling in the July issue cannot be assured that dissemination will not occur. On the other hand, patients without evidence of multiple myeloma 22 and 35 years after histologic diagnosis of solitary plasmacytoma have been described.⁸

Innes and Newall⁹ have reported that 28 of 46 patients with apparently solitary myeloma developed generalized disease, while Tennent¹⁰ found dissemination in 30% of the patients in

his study. Obviously, the number of patients with apparently solitary myeloma who are found subsequently to have disseminated disease will depend on the completeness of the initial examination. Weiner¹¹ found only four instances of long-term solitary plasmacytoma in 563 cases of myeloma.

Treatment consists of irradiation of the involved site after a definite tissue diagnosis has been made. Amputation is not indicated even if the lesion is in the femur or humerus.

True solitary plasmacytoma of bone diagnosed on the basis of (1) histologic proof, (2) absence of any other bony lesion of myeloma, (3) absence of laboratory evidence of multiple myeloma, and (4) adequate follow-up is rare, but I believe that it does exist. The patient with solitary plasmacytoma must be considered suspect for many years, and even then one is never absolutely certain that dissemination will not occur.

Robert A. Kyle, M.D.
Rochester, Minnesota

References

1. Paul, L. W., and Pohle, E. A.: Solitary Myeloma of Bone: Review of Roentgenologic Features, With Report of 4 Additional Cases. *Radiology* 35:651, 1940.
2. Lane, S. L.: Plasmacytoma of the Mandible. *Oral Surg* 5:434, 1952.
3. Christopherson, W. M., and Miller, A. J.: A Re-evaluation of Solitary Plasma-Cell Myeloma of Bone. *Cancer* 3:240, 1950.
4. Pasternack, J. G., and Waugh, R. L.: Solitary Myeloma of Bone: A Clinical and Pathologic Entity. *Ann Surg* 110:427, 1939.
5. Yentis, I.: The So-Called Solitary Plasmacytoma of Bone. *J Fac Radiologists* 8:132, 1956.
6. Kaye, R. L., Martin, W. J., Campbell, D. C., and Lipscomb, P. R.: Long Survival in Disseminated Myeloma With Onset as Solitary Lesion: Two Cases. *Ann Intern Med* 54:535, 1961.
7. Cohen, D. M., Svien, H. J., and Dahlin, D. C.: Long-Term Survival of Patients With Myeloma of the Vertebral Column. *J A M A* 187:914, 1964.
8. Wright, C. J. E.: Long Survival in Solitary Plasmacytoma of Bone. *J Bone Joint Surg [Brit]*, 43:767, 1961.
9. Innes, J., and Newall, J.: Myelomatosis. *Lancet* 1:239, 1961.
10. Tennent, W.: Plasmacytoma of Bone. *Brit J Surg* 32:471, 1945.
11. Weiner, A. D.: Solitary Myeloma of Bone. Thesis, Graduate School, University of Minnesota, 1956.

Viral Encephalitis

EACH YEAR in the late summer and early fall, physicians in the area of the Mississippi Valley see many youngsters and adults who present with an acute encephalitic picture. All too often the exact cause of these illnesses is not delineated, even though efforts are made to isolate the virus or demonstrate a significant antibody rise or both.

Recently, evidence has accumulated that California virus is endemic in this area, and the number of reported cases has increased remarkably over the past several years. Drs. Johnson and Rogers* wisely point out in their excellent article that this rise most likely reflects increased awareness of the California virus rather than a truly increased incidence.

The importance of establishing etiologic diagnoses in cases of apparent viral encephal-

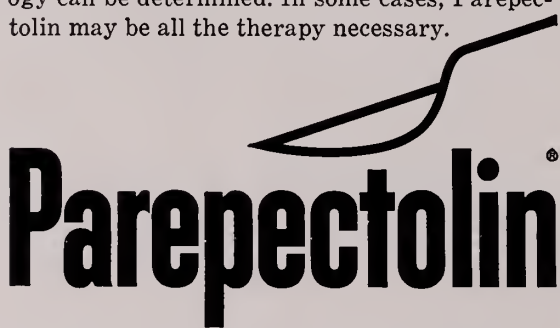
*Johnson, C. M. and Rogers, C. W.: California Encephalitis: Five Cases in Southeastern Minnesota. *Minnesota Med.* 50:1203, 1967.



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itis cannot be overemphasized. This is important not only from the epidemiologic and public health standpoint but also from the standpoint of increasing the understanding of the clinical course of each of the various viral encephalitides. As the authors point out, facilities are now widely available for physicians to pursue these problems to better definition.

Certainly these patients should be carefully studied not only for enteroviruses, herpes, mumps, western and eastern equine, St. Louis, and Powassan viruses, but also for California virus. By doing so the physician should increase his diagnostic achievement considerably.

Robert V. Groover, M.D.
Rochester, Minnesota

Lymphangiography: Value in Determining the Extent of Disease in Patients with Lymphoma*

THE LACK of accuracy which limits the use of lymphangiography for the detection of lymph node metastasis should in no way be misconstrued to discredit the value of lymphangiography in determining the extent of the disease in patients who have lymphoma (Hodgkin's disease, lymphosarcoma, and reticulum cell sarcoma). Gross abnormalities of lymph nodes are detected by lymphangiography, but frequently microscopic metastatic involvement is not detected. Lymphoma, however, usually enlarges the involved lymph nodes and diffusely alters the architecture. Such changes are so definite that they are readily detected roentgenographically after these lymph nodes have been opacified with contrast mediums used for lymphangiography.

Lymphangiography has proved to be the most accurate method for assessment of iliac and retroperitoneal lymph nodes for the presence of lymphoma. In fact, lymphangiography is of such value that the Committee on the Staging of Hodgkin's Disease, at a conference sponsored jointly by the National Cancer Institute and the American Cancer Society (Rosenberg, S. A.: Staging of Hodgkin's Dis-

ease. [Letter to the editor.] Radiology 87:145, 1966) recommended the routine use of lymphangiography for all patients who have Hodgkin's disease to determine the extent of the disease.

Lymphangiography assumes its most crucial role when performed as part of the work-up of patients who have clinically localized lymphoma, stage I or II. Lymphangiograms will reveal lymphoma involving the para-aortic and iliac lymph nodes in some of these patients, a finding which demonstrates that a more advanced stage of disease is actually present.

When initial clinical evaluation shows that a patient has generalized lymphoma, lymphangiography is usually of no practical value because plans for treatment will generally not be altered by the result.

Because lymphangiography is a reasonably accurate method for evaluating the status of the para-aortic and iliac lymph nodes, use of this procedure would seem to be indicated whenever knowledge as to the presence or absence of lymphoma in these lymph nodes would be important in the management of the patient's disease.

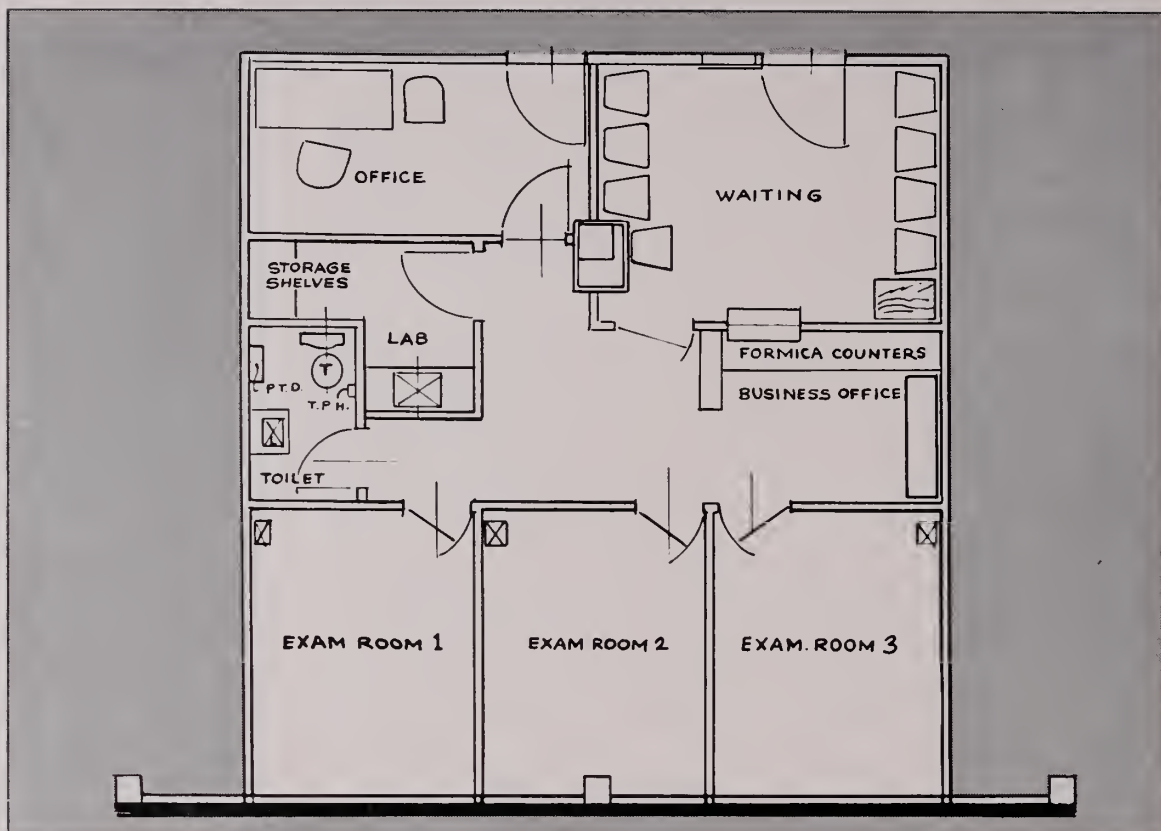
W. Eugene Miller, M.D.
Rochester, Minnesota

*Data based on lymphangiography done on 104 patients with lymphoma. (Unpublished data.)

Sigel, M. E.: Cervical Lymphography. Minnesota Med 50: 1035, 1967.

Don't tell me what you dreamed last night for I've been reading Freud.
—Franklin Adams

Anybody can win, unless there happens to be a second entry.
—George Ade



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Respiratory Mucosa*

THE ROLE OF the respiratory mucosa is a very interesting one indeed and has received a great deal of attention both from the examination of human material and also from experimental studies. Probably the most significant study is the compilation of material accumulated by the Surgeon General's Committee on Smoking and Health. Although there is much discussion today on the role of air pollutants and their effect on the respiratory epithelium, cigarette smoke has been found to be by far the most damaging.

Non-Carcinogenic Changes

The inhalation of foreign material into the tracheobronchial tree is capable of causing a variety of changes. Basically there are two types of changes which are found following such exposure. If the agent is non-carcinogenic the changes in the tracheobronchial tree will be those of basal cell hyperplasia in which the basal cells have nuclei uniform in size and shape without any definite alteration in the chromatin content. The increase in cells is uniform and orderly, and the cilia on the surface are also unaltered. In response to such stimuli there may also be a loss of cilia with a flattening of the cells on the surface with their nuclei at right angles to the long axis of the tracheobronchial tree. The transformation into this type of epithelium is that of squamous epithelium similar to that which lines the pharynx or mouth. Keratinization on the surface is a rare occurrence in the tracheobronchial tree.

Carcinogenic Changes

Far more important and far more significant are the changes produced by carcinogenic agents, the most important of which result from cigarette smoking. Although the specific elements have not been completely isolated from the cigarette, nevertheless, it is the inhalation of the cigarette smoke that causes

changes found to be present in the basal cells. Here the nuclei undergo alterations in size and shape, irregular condensations of the chromatin and clumping of the chromatin. These cells migrate toward the surface and replace the normal epithelial cells as they progress toward the surface. As the proliferation progresses and the changes become more extensive, the cells take on the characteristic appearance of carcinoma cells.

Carcinoma In-Situ

As the process continues, these atypical cells migrate toward the surface and, with a disappearance of the cilia on the surface, a change occurs which may be designated as carcinoma-in-situ. It is of interest that the inhaled carcinogenic agent produces these changes in all parts of the tracheobronchial tree. The areas of carcinoma-in-situ are frequently present at the sites of bifurcation and least frequently observed in the trachea. In subsequent stages early invasion occurs at the site of carcinoma-in-situ, with the penetration of the basement membrane and extension into the underlying tissue. These invasions are observed more frequently in cases of bronchial carcinoma but are also present in cases where no carcinoma of the bronchus is found. It is of interest that the same changes observed in the epithelial lining of the bronchus are present in the bronchial glands. In some instances the epithelial perforation extends to the surface with a disappearance of all the normal elements within the bronchial glands. Carcinoma-in-situ is also absent in the glands but not early invasion.

Effects of Discontinuing Smoking

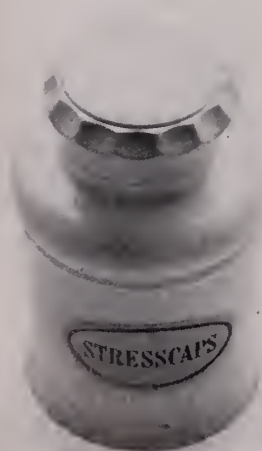
Another interesting feature is the regression of changes which occur after individuals stop smoking. A study was done in which 72 cigarette smokers were compared with 72 men who had smoked for at least ten years and had then given up the smoking habit for at least five years. These two groups were compared with another group which had never smoked regu-

*Hilding, A. C.: The Role of the Respiratory Mucosa. Minnesota Med 50:915, 1967.



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larly. In all three groups the men were matched as to age, locality and, where possible, occupation. Several interesting findings were observed. There were no zones of carcinoma-in-situ in the individuals who had never smoked. There was a precipitous drop in the areas of carcinoma-in-situ in the former cigarette smokers when compared with men of the same age and same smoking habits who continued to smoke. There was also a precipitous drop in

*Senior Medical Investigator, Veterans Administration.

the number of atypical cells in those who had given up the cigarette habit in comparison with those who continued to smoke.

There is sufficient evidence from the pathologic studies to support the views expressed by Dr. Hilding in his article and to state unequivocally that cigarette smoking today is the single most important factor in the development of lung cancer.

Oscar Auerbach, M.D.*
East Orange, N. J.

Test Your Word Score

Intraluminal—*within the lumen of a tube* (page 1617).

Acupuncture—from Latin *acus* (needle) + *punctura* (a pricking)(page 1622).

Deleterious—*hurtful; injurious* (page 1626).

Olfactory nerve—*first cranial; forebrain* (page 1632).

Sham rage—*quasi-emotional fear plus anger upon trifling provocation*(page 1633).

Telangiectasia—*a condition characterized by dilatation of the capillary vessels and minute arteries, forming a variety of angioma* (page 1679).

Dysesthesia—*impairment of sensation* (page 1684).

Comparison

The surgeon knows everything and does everything. The internist knows everything and doesn't do anything. The psychiatrist doesn't know anything and doesn't do anything.

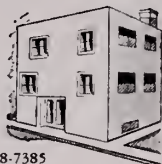
—Anon.

Caesarean operation has no relation to the birth of Julius Caesar. The term goes far back into antiquity, and the operation is supposed to have been performed by the early Greeks. The word "Caesarean" derives from the Latin past participle, caesus, from caedere, meaning to cut.

—Liberty

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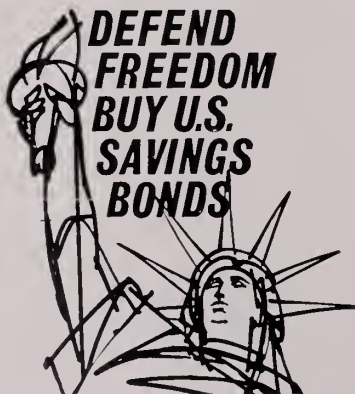
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You May Be Right

AT THE RISK of being labelled a bigoted crank, may I take exception to certain statements in an editorial in the January 1967 issue of *Minnesota Medicine* entitled "Why Therapeutic Abortion?" by Theodore Watson.

1. "Saint Thomas Aquinas in the 13th Century held that the soul was directly created by God and infused in the embryo, not at the point of conception, but when the embryo was sufficiently formed to receive it."

Thomas Aquinas described three types of souls: The vegetative, the sensitive and the intellectual soul. He further states that these are "numerically one and the same soul."¹ He did not approve abortion before the development of the intellectual or rational soul.

2. "This allowed the Medieval Church to forbid abortion only after quickening."

There is no historical evidence that the Roman Church ever condoned or acquiesced in abortion at any stage of gestation. Theologians have defined feticide as murder, if the fetus has a human soul. Varying estimates of the moment of ensoulment originate from earliest times. Fourth century theologians, such as St. Basil² and St. Gregory of Nyssa,³ held that the soul was infused at the time of conception and that all abortion was homicide. This concept is not exclusively a "relatively modern one."

In two ways the Church Fathers have proscribed abortion before ensoulment or without direct reference to ensoulment. Since the development of the child from conception to birth terminates with development of human life, direct interference with this process is forbidden by the Natural Law; secondly, by the application of the Principle of Indeterminacy, human life may be present at any point in gestation, and the abortionist must take full responsibility for this possibility.

The Papal Bull, *Effraenatam* by Sixtus V, issued on October 29, 1588, defined severe ecclesiastical penalties for abortion as well as for contraceptive practices. According to Noonan,⁴ Gregory XIV repealed all portions with the exception of abortion of an ensouled, forty-day fetus in the Papal Bull, *Sedes Apostolica*, May 3, 1591. This did not in any sense allow abortion earlier than forty days.

It may be a fair statement that direct abortion before ensoulment was not considered homicide by some Church Fathers (St. Augustine) and possibly a lesser evil with lesser penalties. However, it is not correct to imply that the Church ever considered early abortion anything other than a serious evil.

3. "Pope Gregory V in 1591 designated quickening to occur after 116 days."

Gregory V died in 999. The reference is probably to Gregory XIV, as discussed previously.

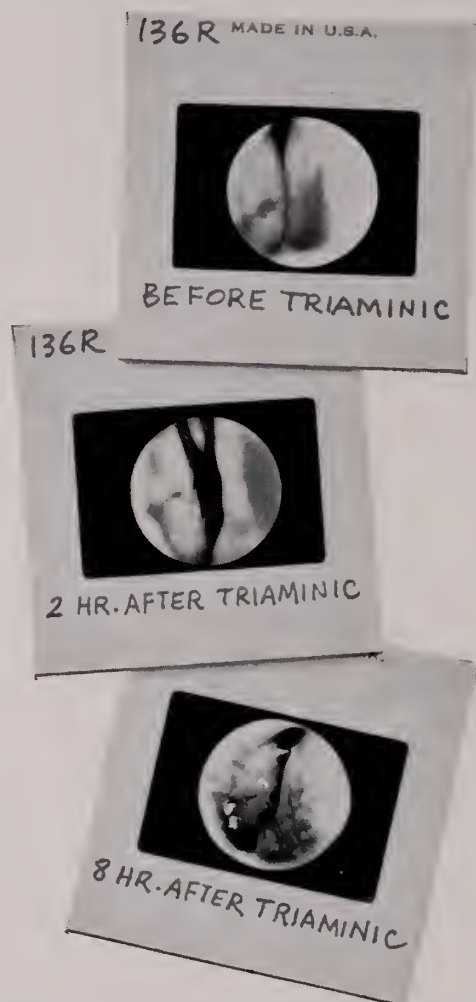
In my opinion, it is regrettable that these inaccuracies have appeared in print, especially when they have been quoted verbatim by the local press as authentic historical facts.

Raymond J. Albrecht, M.D.
St. Paul, Minnesota

References

1. Summa Theologica, Q.76, Article 3.
2. Abortion and Public Policy, Shaw, R. B., Pa. 48, 1966.
3. Catholic Encyclopedia, Vol. 1, Pa. 47, 1901.
4. Contraception, Noonan, John T., Pa. 362, 1965.

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The Editor's Soliloquy

The Cults

A system for the cure of disease based on dogma set forth by its promulgator can scarcely qualify as an indispensable health service, nor should any recipient of government benevolence under Medicare be free to choose a system of therapy neither substantiated nor sanctioned by scientific medicine.

If we are to continue to operate a government for the benefit of the people, that government should feel obligated to protect us against health fallacies as well as against other forms of exploitation and chicanery. In the public interest do we not now have such agencies as the Interstate Commerce Commission, the Food and Drug Administration, the Federal Trade Commission, and others operating in their respective fields to protect us from abuses against which we could not individually defend ourselves?

The gamut of health cults runs from ingenuous faith healing to calculated fraud; there have been and may still be extant such "follies" as Autohemic Therapy, Poropathy, and Bio-Dynamo-Chromatic Diagnosis and Therapy, plus 1001 other pseudo-medical practices with no scientific validity. There are pathetically misguided persons who have profound but blind confidence in a copper wire bracelet or a "rheumatism ring" to prevent, alleviate, or cure arthritis; some fanatics ascend 150 steps or more on their knees to reach "miracle" altars or shrines for the cure of their ailments; other gullibles patronize the bonesetter, massager, the mesmerist, or the mere layer-on-of-hands; even the arcane rites of the voodooist or the necromancer can still attract a minority clientele.

Submitting oneself to any type of illegitimate therapy is the prerogative of the individual; but a government should not use tax revenue to support and thereby indirectly endorse such cults. Irrelevant to the issue is the fact that some legislatures may approve licensure of some of the cults.

It is significant that the cults which have been licensed by state legislatures, received the privilege to a limited practice many years ago when the gap between the abilities of the cultists and the medical knowledge of the day was not so wide nor so regrettable as current remarkable developments in scientific medicine have made it today.

It would seem that if many of our honorable United States senators are unwilling to commit themselves unequivocally on this important issue: namely, that of safeguarding their constituents' welfare in the medical field, we may have to become dubious of their sincerity and competence in other areas. Are we to assume that they have not conscientiously informed themselves on this crucial matter, or that they have yielded to the pressures of wily lobbyists? And this despite the fact that experts have advised them that medical cults have no sound scientific basis and should therefore be excluded from the health services eligible for government support!

This is no area for congressional compromise!—Carl O. Rice, M.D.

Old Doc Hess says: Allow those who are familiar with a subject to have their say; they may speak softly—so listen closely!—COR

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Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Pyrazole compounds may potentiate the pharmacologic action of sulfonyleurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and report immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage occur. Make regular blood counts. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

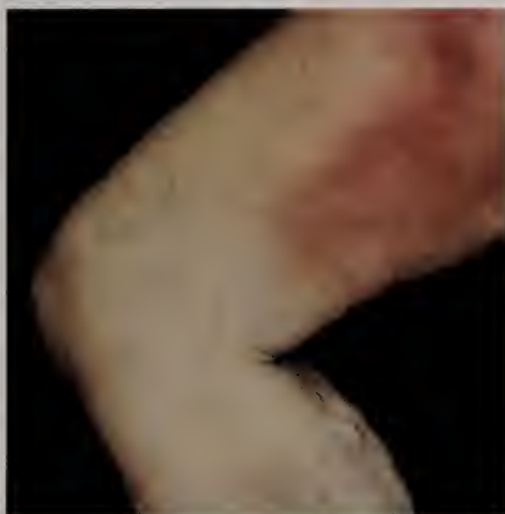
Adverse Reactions: The most common are nausea, edema and drug rash. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately before or after meals or with milk to minimize gastric upset. Mild drug rashes frequently subside with reduction of dosage. However, rash accompanied by fever or other systemic reactions usually requires withholding medication. Purpuric rash has also been reported. Agranulocytosis, exfoliative dermatitis, Stevens-Johnson syndrome, or a generalized allergic reaction similar to serum sickness may occur and require permanent withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

Dosage in Acute Superficial Thrombophlebitis: Initial: 6 capsules or tablets daily in divided doses for 2 or 3 days. Maintenance: 3 capsules or tablets daily. Usual duration of therapy is 5 to 7 days (rarely beyond 10 days). 6509-V(B)R2

*Stein, I.D.: Presented at the American Academy of General Practice, Dallas, Sept. 1967.

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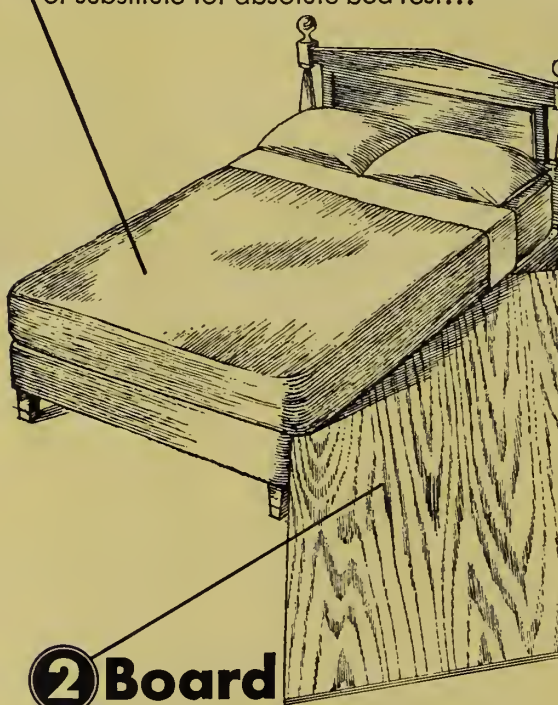
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LOW-BACK PAIN

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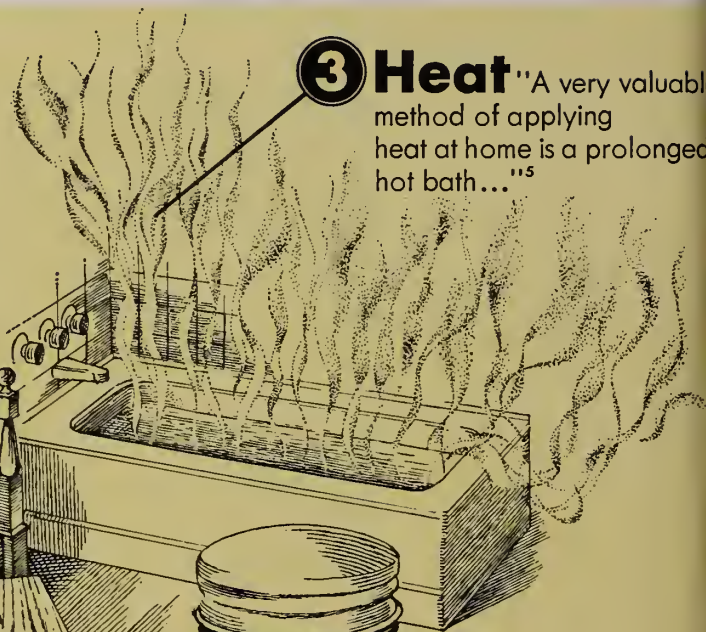
The low back pain that is most frequently seen in general practice is mechanical in nature, i.e., postural back pain, joint dysfunction and acute back strain.^{1,2} For this type of discomfort, a conservative regimen is usually sufficient to relieve aches and pains, and to help keep the patient functioning. Components of this basic program include:

1 Bed "If the patient is in the pain-spasm-cycle...there is no alternative or substitute for absolute bed rest..."³



2 Board "Boards should be ordered under the mattress...these boards act by immobilizing the spine..."⁴

3 Heat "A very valuable method of applying heat at home is a prolonged hot bath..."⁵



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References: (1). Godfrey, C.M.: *Applied Therop.* 8:950, 1966. (2). Gottscholk, L.A.: *GP* 33:91, 1966. (3). Rowe, M.L.: *J. Occup. Med.* 2:219, 1960. (4). Cozen, L.: *South Dakota J. Med.* 18:26, 1965. (5). Soto-Holl, R.: *Med. Sc.* 14:23, 1963. (6). Weiss, M. and Weiss, S.: *J. Am. Osteopath. A.* 62:142, 1962. (7). Feuer, S.G., et al.: *New York J. Med.* 62:1985, 1962.

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Curbstone Consultation

QUESTION: If Hodgkin's disease starts with skin lesions, are there any diagnostic characteristics of such eruptions?

A 56-year-old cattleman developed an acute erythema of both arms and forearms after exposure to 2-4-D. The pruritus was severe. The eruptions subsided with the administration of steroids and local application of olive oil. As the skin lesions subsided, he developed anorexia, nausea, vomiting, weakness, weight loss and leucocytosis. Chest x-rays, upper and lower gastrointestinal studies, intravenous pyelogram, blood serology, sternal puncture, gallbladder x-ray, and brain scan were all negative. Finally, eight months after appearance of the skin lesions, a small supraclavicular node appeared on the right side. Biopsy established the diagnosis of Hodgkin's disease. Did 2-4-D have anything to do with the Hodgkin's?

ANSWER: When Hodgkin's presents itself as a skin disease (lymphogranulomatosis cutis), the skin lesions may be specific or non-specific. The specific lesions may be circumscribed infiltrations or papules appearing in groups on the extremities or the trunk. The histologic changes in these lesions are the same as those found in the lymph nodes of Hodgkin's disease. The non-specific lesions may be urticarial, vesicular, erythematous or may resemble erythema multiforme; exfoliative glossitis may occur. The non-specific lesions may precede or accompany lymph-node enlargement.

It is impossible to state that there is a causal relationship between 2-4-D and the diagnosis of Hodgkin's disease. It would appear that because this substance was used prior to the eruption it was a suspected cause, but not a proven one. There were no patch tests applied; there was no involvement of the face or generalized eruption. According to toxicologists this chemical has a low degree of toxicity. Furthermore, if one were to give an opinion on these meagre facts and state that the material used was the cause of Hodgkin's disease it would have grave legal implications. There are many systemic diseases which have a non-specific cutaneous manifestation, both at onset and concomitant with the symptoms. It is also true that some have specific eruptions which can be demonstrated as such by biopsy. In other words, I don't think I am being of much help, except for giving one man's opinion!

Elmer M. Rusten, M.D.
Minneapolis, Minnesota

Philosophers are people who talk about something they don't understand, and make you think it's your fault.

—Jacob Braude: *Speaker's Encyclopedia*

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The Viewing Box

Cough and Hemoptysis in a Nineteen-Year-Old Female

THE PATIENT was a 19-year-old white female, who was admitted to the hospital with complaints of weakness, fatigue, lethargy and arthralgia of approximately one month's duration. These symptoms had become progressively worse, and two days prior to admission there was onset of cough, hemoptysis, dyspnea and fever. Physical examination on admission revealed a pale, young white female, moderately dyspneic, with constant coughing productive of bloody-tinged mucoid sputum. Temperature was 103°, respiration rapid, and pulse 140 and irregular. Multiple rales and tubular breathing were heard throughout both lung fields. A tachycardia was present, but no murmurs were heard. Examination of the extremities and abdomen was essentially negative.

Hemoglobin on admission was 4.4 grams per cent with a hematocrit of 15.5 volumes per cent. The white blood count was 12,000 with 91 per cent P.M.N.s, 7 per cent lymphs and 2 per cent monos. Urinalysis revealed smoky appearance, pH. of 5, specific gravity of 1.013, albumin of 4 plus, 5 to 8 white blood cells per high power field and a full field of red blood cells per high power field. Occasional granular casts were also seen. BUN was 87 milligrams per cent. Sputum cultures revealed a moderate number of yeasts, biochemically and morphologically indistinguishable from *Candida albicans*.

Chest roentgenogram (Figure) revealed presence of large confluent areas of density in both lung fields extending outward from the hilar region with the apices and extreme lung bases relatively spared. No pleural effusion was seen. Cardiac size was felt to be within normal limits.

Blood transfusions were given, and the patient was placed on penicillin, chloromycetin and solu-cortef. She remained febrile during the first two days of hospitalization; then the temperature returned to normal. Her cough, dyspnea and hemoptysis progressively worsened, and on the fourth hospital day she expired.

What is your diagnosis? (See next page.)



Figure

Diagnosis: Goodpasture's syndrome.

Autopsy was performed and a subacute exudative and proliferative glomerulitis accompanied by a necrotizing pneumonitis with massive intra-alveolar hemorrhage was found.

The confluent large areas of density in the lung fields seen on admission chest roentgenogram represent massive intra-alveolar hemorrhage. Radiographically, differentiation from other causes of massive bilateral pulmonary consolidation may be difficult, although the relative sparing of the bases and apices may be a helpful differential point. Correlation with clinical findings and history is necessary for diagnosis.

Discussion

Since Richard Bright's classic description of glomerulonephritis in 1836, it has become apparent that histologic glomerular lesions portray a spectrum of diseases with different etiologies and pathogenetic mechanisms. One such variant was first recorded by Goodpasture in 1919, in a study of the pulmonary lesions of influenza. The case was that of a young man who, when recovering from an influenzal attack, had hemoptysis, anemia and albuminuria, and died. Autopsy showed marked pulmonary alveolar hemorrhage and proliferative glomerulonephritis. Stanton and Tange in 1958 reported nine cases of pulmonary hemorrhage associated with glomerulonephritis and suggested the term Goodpasture's syndrome. Since then, there has been a sufficient number of cases reported presenting this disease complex to warrant its being regarded as a specific entity.

The underlying disease process has yet to be clarified. Some have suggested that the changes may be secondary to generalized hypersensitivity reaction which produces an acute necrotizing alveolitis, resulting in repeated episodes of pulmonary hemorrhage. Various drugs including penicillin and antigens have been implicated as possible causative agents. Others have suggested that a pre-existing streptococcal infection might serve as an etiologic factor. The similarity between the pulmonary manifestations of this entity and idiopathic pulmonary hemosiderosis has led to the suggestion that the two conditions may actually represent manifestations of the same pathologic process.

The syndrome predominates in males 9 to 1, and the median age at onset is 21 years. Hemoptysis is the initial symptom in most cases reported and varies from slightly blood-streaked sputum to massive hemorrhage, tending to occur in bouts. Dyspnea and cough are also prominent symptoms. Anemia is always present, even early in the course of the disease. Azotemia is noted late in the disease. Albuminuria and microscopic hematuria are almost always present. Granular casts in the urine have been seen in approximately 50 per cent of the previously reported cases.

The roentgenographic appearance of the lungs is basically the same as that observed with idiopathic pulmonary hemosiderosis. During the acute episode of hemoptysis, there are ill-defined multiple nodular or flocculent densities bilaterally with a perihilar distribution and tendency to spare the apices and bases. These changes may disappear within a few days. Chest roentgenograms taken between the acute episodes show an increase in the interstitial markings characterized by finely granular-appearing reticular accentuation throughout the lungs.

Characteristically, Goodpasture's syndrome is a rapidly fatal disease occurring almost always in young adult males. The median duration of the illness is

about 15 weeks. In absence of specific therapy, steroids have been widely used but the results have often been disappointing. However, there are several reported cases in which steroids have been beneficial in arresting the disease process.

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William J. Boardman, M.D.*
Minneapolis, Minnesota

References

1. Sybers, R. G., M.D., Ph.D., et al.: Roentgenographic Aspects of Hemorrhagic Pulmonary-Renal Disease (Goodpasture's Syndrome). *Amer J Roentgenol* 94:674, 1965.
2. Benoit, F. L., LCDR., MC, USN, Rulon, D. B., Capt., MC, USN, Theil, G. B., M.D., Doolan, P. D., CDR., MC, USN, and Watten, R. H., CDR., MC, USN. Goodpasture's Syndrome, a Clinico-Pathologic Entity. *Amer J Med* 37:424, 1964.

Corpse Blood Transfusion

Take a large medical institution in a big city; say, some first-aid hospital. Look in at the reception ward. You will see that the doctor there is in great demand.

Now picture the doctor on duty, the doctors in the wards, their assistants, and the professor who heads this beehive of activity. They scarcely have time to step away from the operating table.

And late at night a man is brought in who accidentally fired off his gun, and injured himself. The bullet penetrated his abdominal cavity.

The professor takes the man's pulse. It is barely perceptible. There are signs of internal hemorrhage . . . An urgent operation is necessary to suture the injured organs and vessels. An immediate blood transfusion must be made at the same time; if this is not done, the case is hopeless.

All the preparations have been completed. The donor is summoned and is expected at any moment (blood conservation was not known at the time).

But the patient's condition suddenly takes a sharp turn for the worse. The transfusion must be made without further delay. Yet the donor is still on his way.

A daring idea suddenly strikes the professor. A man knocked down by a car has just been brought to the reception ward. He was still alive when he arrived, but dies soon afterwards in spite of the fight they put up for his life. The professor decides to take the blood from the dead man and transfuses it to the gunshot victim.

It is all over within an hour: the operation, and the transfusion as well. The patient's pulse grows stronger as the heart pumps the blood taken from the corpse to all the parts of his body. Certainly, the blood of both the patient and the corpse was tested for compatibility before the transfusion.

All this, but for some minor details, is a true story. It happened at the Moscow Sklifosovsky Institute in 1930.*

*L. Fridland, M.D.: *The Achievement of Soviet Medicine, 1961*, edited and translated from the Russian by W. Horsley Gantt, M.D.

Sneezing

Whence comes the custom of blessing and saying "God help" to those that sneeze? We produce three sorts of wind: that issuing from below is too indecent; that from the mouth implies some reproach of gourmandizing; the third is sneezing. And because it comes from the head, and is without imputation, we thus kindly entertain it.

—Michel de Montaigne



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antihypertensive agents by at least one-half.
Diuretics, narcotics or alcohol may po-
tentialize hypotension. Because of the possi-
bility of progression of renal damage, peri-
odic determination of the BUN is indicated.
Discontinue if the BUN rises or liver dysfunc-
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precipitated.

Electrolyte imbalance, sodium and/or potas-
sium depletion may occur. If potassium deple-
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should be discontinued and potassium sup-
plements given, provided the patient does
not have marked oliguria.

Special care in cirrhosis or severe
congestive heart disease and in patients re-
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Fluid restriction is not recommended.

Side Reactions: Nausea, gastric irritation,
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ing, dizziness, weakness, restlessness, hy-
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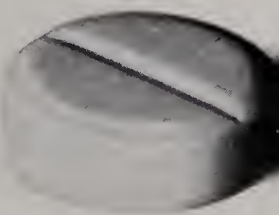
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Tumor Conference

Hemangiomatosis of the Small Bowel

ALTHOUGH HEMANGIOMAS are frequently found in various areas of the body, they rarely involve the gastrointestinal tract. A review of the literature in 1964 by Dwyer revealed only 200 cases of intestinal hemangiomas reported over a 100-year period.¹ Gentry reviewed 1,400,000 case records at the Mayo Clinic and found only 106 cases of vascular lesions involving the intestine.² Although intestinal hemangiomas frequently bleed, rarely are they considered in the differential diagnosis of gastrointestinal hemorrhage.

Recently we had an occasion to treat a patient with multiple diffuse hemangiomata of the small bowel at the University of Minnesota Hospitals. The purpose of this communication is to present the pertinent clinical features of this case and to briefly discuss the management of multiple diffuse telangiectasia* of the small intestine. Particular emphasis is given to the need for surgical resection of the involved bowel in those patients in whom the disease has resulted in chronic disability or even a threat to their life.

Case Report

A 49-year-old bus driver was admitted to the University of Minnesota Hospitals on June 10, 1966, with a three-day history of rectal bleeding and melena and a falling hemoglobin despite the administration of eight units of whole blood at an outside hospital. His past history revealed that he had had two similar episodes in the past, once in 1963 at which time he required the administration of 10 units of whole blood for painless rectal bleeding. A rather extensive course of investigation in 1963 including an x-ray examination of the upper and lower gastrointestinal tract revealed no apparent cause for gastrointestinal hemorrhage. He had no symptoms suggestive of peptic ulcer disease or esophageal varices. After the initial episode in 1963 he enjoyed a symptom-free interval until March 1965, at which time he again sustained a massive hemorrhage. After the administration of eight units of blood an exploratory laparotomy revealed multiple small hemangiomata involving the entire jejunum. The remaining abdominal organs were normal. A 13-cm. segment of proximal jejunum was resected and histological examination confirmed the presence of capillary telangiectasia.**

He continued to do well until June of 1966 when melena recurred. Each of the three bleeding episodes was heralded by sudden weakness and fainting, a particularly treacherous situation for a bus driver. On arrival at the University of Minnesota Hospitals his hemoglobin measured 7 Gm. %; his blood pressure was 130/70 and pulse 120. Physical examination revealed a well-developed male with no other evident abnormalities except the pronounced anemia and melena. Gastric aspiration revealed no blood although he

*See Test Your Word Score Page 1659.

**The exploratory laparotomy was carried out by Dr. C. M. Phibbs, Jr., at St. Barnabas Hospital, Minneapolis, Minnesota.

was actively bleeding. During the ensuing three days he received 11 units of blood and his hemoglobin stabilized at 13 Gm. %. A selective superior mesenteric and celiac arteriogram revealed no evident abnormalities. Because of the insidious onset of the bleeding episodes and because of the serious consequences in his occupation as a bus driver, the decision to operate upon this man was made in the hope of being able to resect most, if not all, of the involved small intestine.

On June 21, 1966, the patient was taken to the operating room and the abdomen was explored through a midline incision. The stomach, duodenum, and the proximal three inches of jejunum were entirely normal, as was the colon. However, the remainder of the jejunum was studded with multiple small hemangiomas measuring from one to 10 mm. in diameter (Figure 1). After carefully measuring the entire length of the small intestine it was found that the distal eight feet of ileum were free of disease. Except for the most proximal two inches all of the jejunum was resected and a jejunal-ileostomy in a single-layer closed anastomosis was carried out. The patient's postoperative course was entirely uneventful and he was discharged from the hospital on June 27, 1966.



Fig. 1. Intra-operative photograph of small bowel revealing multiple small hemangiomas.

Examination of the removed specimen revealed an eight-foot length of jejunum with multiple hemangiomas, the largest measuring one cm. in diameter, with a small mucosal defect. Microscopic examination of the hemangiomas revealed multiple vascular spaces lined with endothelium; the appearance was consistent with a diagnosis of multiple hemangiomas of the small bowel. The patient was subsequently seen on several occasions in the outpatient department. His only complaint in the early postoperative period was that of three to four loose bowel movements per day, but on his last visit in January of 1967 he stated that he had one formed stool per day. His hemoglobin was 14.2 Gm. % at that time and he had had no recurrence of melena since his operation. The patient again is gainfully employed as a bus driver.

Discussion

Several classifications of vascular lesions involving the gastrointestinal tract have been described, the most common being that proposed by Kaijser, who classified intestinal hemangiomas into four different groups.³

Multiple Phlebectasia

This form of hemangioma usually involves the small bowel, and on microscopic examination large channels are seen which are similar to those seen in the cavernous variety. However, the vascular walls are usually thicker and contain a variable amount of smooth muscle, and the lumen frequently communicates with the sub-mucosal veins. The lesions are nearly always multiple and small and may involve large segments of the intestine. If symptomatic, their presence is usually signified by anemia, melena or painless rectal bleeding.

Cavernous Hemangioma

Cavernous hemangiomata usually involve the large bowel with preference for the sigmoid colon and rectum and may occur either in a diffuse form or in a more circumscribed polypoid variety. Microscopically, the vascular walls do not contain smooth muscles and the histological picture is that of large blood filled spaces lined by round or flat endothelial cells. Though hemorrhage is the most frequent symptom, occasionally they have given rise to large bowel obstruction.

Capillary Hemangioma

This type of hemangioma usually occurs as a single discrete sub-mucosal nodule which at times may become pedunculated. Hemorrhage or intussusception has usually led to a diagnosis of this lesion.

Hemangiomatosis or Multiple Diffuse Telangiectasia

This term implies a manifestation of a widespread disease and on occasion is associated with hemangiomata of the skin and other sites. The clinical setting of this lesion is usually one of long duration before the correct diagnosis is made and is characterized by multiple severe gastrointestinal hemorrhages, anemia, and occasionally even obstruction and intussusception of the bowel. The case presented in this report falls into this group.

Discussion

From a brief review of the literature it would appear that no age group is exempt. In 1966 Nader and Margolin reviewed 48 cases of intestinal hemangiomata in children, including one case of their own.⁴ The average time between the onset of symptoms and the correct diagnosis in their report was 16 years with a range of 0 to 49 years. The bleeding episodes were usually intermittent and sometimes marked by long periods of remission.

The diagnosis of vascular malformation as a cause of gastrointestinal bleeding is largely a diagnosis of exclusion. Intestinal hemangiomatosis has no distinguishing radiological or laboratory features. Occasionally the presence of an extra mucosal filling defect or the presence of phleboliths outside of the pelvis should raise the suspicion of vascular malformation. The diagnosis of intestinal hemangiomatosis may at times be difficult even at operation. Usually the lesions are quite striking when encountered, but may be almost invisible, especially after the bowel has been handled or if active bleeding is present.

As has been stated by Vetto, the tendency for spontaneous remission renders the evaluation of any treatment difficult.⁴ Radiation therapy and injec-

tion of sclerosing agents have not been of any value. In many instances the disease has run a relatively mild course and the administration of blood transfusion and iron have remained the mainstay of treatment. However, in those instances where repeated massive hemorrhages have led to prolonged disability and a threat to life, extensive resection of the involved bowel appears to be justified. Vetto reports four patients who underwent a 50% resection of the small intestine after failure of conservative management.⁵ Two of these patients have had no further evidence of bleeding. In one patient the severity of bleeding had been markedly reduced and in the fourth patient recurrent hemorrhage requiring multiple transfusions occurred.

The patient described in this report has had no further bleeding since his operation, and in view of the serious disability associated with the previous hemorrhages, a 50% resection of the small intestine appears to be fully justified. Since all of the involved small bowel was removed, the likelihood of subsequent recurrence is indeed remote.

Summary

The case of a 49-year-old male with multiple diffuse telangiectasia of the jejunum is presented, who underwent a resection of one half of his small bowel for recurrent life-threatening and disabling hemorrhages. It is suggested that surgical resection of the involved segments of intestine offer the only chance for definitive cure. However, it should be emphasized that large resection should be reserved for those patients whose bleeding is severe and life-threatening.

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References

1. Dwyer, W., Jr., and Steinlauf, P.: Surgical Implications of Intestinal Hemangiomas. *Post Grad Med* 36:330, 1964.
2. Gentry, R. W., Dockerty, M. B., and Clagett, T. O.: Vascular Malformations and Vascular Tumors of the Gastrointestinal Tract. *Surg Gynec Obstet* 88:281, 1949.
3. Kaijser, R.: Ueber Hemangioma des Tractus Gastrointestinalis. *Arch Klin Chir* 187:351, 1936.
4. Nader, P. R., and Margolin, F.: Hemangioma Causing Gastrointestinal Bleeding. *Amer J Dis Child* 111:215, 1966.
5. Vetto, R. Mark: The Management of Multiple, Diffuse Telangiectasia of the Small Intestine. *Surg Gynec Obstet* 115:55, 1962.

Bilateral Posterior Lobe Cerebellar Syndrome

Involvement of both posterior lobes of the cerebellum causes dysarthria, marked involvement of gait, and an inability to carry out skilled, voluntary movements on either side. Likely etiologic factors include infections, such as chronic encephalitis, and degenerative or demyelinating lesions, such as multiple sclerosis. Less frequently, tumors may be a cause.

Durham, Robert H.—*Encyclopedia of Medical Syndrome*
Hoeber Medical Division, Harper and Row, New York

California is a fine place to live in—if you happen to be an orange.

—Fred Allen



Neurological Conference

Diabetic Neuropathy*

Dr. Steve Drosman:**

The patient is a 24-year-old man complaining of burning and tingling in his legs. He had had symptoms of fatigue, weight loss, polydipsia, and polyuria for about 10 years; however, he did not consult his physician until four and one-half years ago. At that time a diagnosis of diabetes was made and he was started on orinase. Since he failed to improve, he was started on 20 units of protamine zinc insulin. After vacationing for a month, he returned even more fatigued, and his private physician increased his dose of protamine zinc insulin to 40 units. He has remained on this amount for the past four years. During this time the patient did not regulate his diet or attempt to maintain an adequate control of his diabetes.

In April, 1965, the patient had a flu-like episode with high temperature, nausea, vomiting and a great deal of bloating. Chest pain was also present. Upon hospitalization his blood sugar was 675 mg.%. Lente insulin was initially started at 80 units, and eventually reduced to 45 units upon dismissal from the hospital. Towards the latter part of April, 1965, the patient started complaining of burning and cramping pains in his legs and feet. When questioned further about these symptoms, he stated that these pains had been present intermittently for the preceding four years, but neither as severe nor as constant. Increasing neurological symptoms necessitated rehospitalization in June, 1965. Vitamin B-12 therapy was given for 10 days without obvious benefit. His insulin was readjusted at that time to 50 units of lente and 10 units of semilente. In addition he was placed on an 1800 calorie diabetic diet when he was sent home from the hospital. When he left the hospital in June, his normal weight of 150 pounds had decreased and stabilized at 120 pounds, the loss apparently having occurred during the prior six to seven months.

Physical Findings

On physical examination his general appearance was that of a tall, thin young man in no acute distress. The vital signs including blood pressure were normal. Examination of his mouth revealed gingivitis and carious teeth. The heart and lungs appeared to be normal, as was the abdomen. Examination of his extremities showed a reduced muscle tone of the soleus and quadriceps bilaterally, although his strength and coordination appeared normal. The deep tendon reflexes were somewhat sluggish but equal bilaterally. There was a definite hypesthesia and hypalgesia extending from the knees and increasing distally. The cranial nerves were normal. Funduscopic examination revealed no abnormalities of the eye grounds.

Laboratory Studies

The initial lab work revealed a normal complete blood cell count and sedimentation rate, and a 4+ urine sugar and acetone; however, a repeat check noted no urine acetone. The initial blood sugar was 315 mg.%; the serum cholesterol was 220 mg.%; and the serum triglycerides were 165 mg.%, the normal range being 130-135 mg.%. The chest x-ray and electrocardiogram were also within normal limits.

Progress

In diabetic clinic a 2400-calorie low-fat diet was prescribed together with 50 units of lente

*Neurological Conference held November 9, 1965. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals.

**Student doctor, University of Minnesota Hospitals.

and 10 units of semilente daily. A neurological evaluation considered the sensory loss to be a peripheral neuritis secondary to diabetes; and thiamine 100 milligrams three times weekly intramuscularly and multivits were recommended. His burning dysesthesias* continued unabated at home, and when he returned to the Neurology Clinic on October 18, 1965, it was felt that he should be admitted for more intensive care.

The Evaluation

Medical Evaluation

Dr. Gerald Lee:**

Poor dental hygiene could be a cause for poor control. The patient has multiple *dental caries*. Secondly, although he does not appear to have an occult hidden infection, when diabetes is not well controlled, an infection should be suspected. I would recommend obtaining repeat chest x-rays with apical lordotic views, and a complete blood count. We are checking the 7 a.m. temperature daily but, as *tuberculosis* characteristically produces an evening temperature, I would favor taking two or three temperatures per day. Williams¹ makes the point that a diabetic patient may develop an *allergic reaction* to beef insulin which may be responsible for nerve damage and hence aggravate or cause diabetic neuropathy.

Future Problems

Although diabetic neuropathy is the patient's main complaint now, we might also consider future problems that will probably arise.

With the advent of insulin, diabetes is a different disease, since patients survive longer to suffer or expire from vascular complications. Williams and others also have recently emphasized that disturbance of fat metabolism is very common among diabetics. Most diabetics have hypercholesterolemia or hypertriglyceridemia or both and thereby premature atherosclerosis. Fatty acid metabolism is now thought to be closely related to the beta chain of insulin. The alpha and beta chains are split as they are being utilized; the beta chain is thought to be a stimulus for fatty acid synthesis. Patients less frequently develop allergic reactions to pork insulin. Since coronary heart disease and peripheral vascular disease are the major problems that confront the diabetic with increasing years, each diabetic should try to reduce known risk factors. Smoking is very harmful. Hypertension should be controlled, and causes for an increase of blood pressure should be established and corrected if possible. Hyperlipemia also should be reduced, if possible, by diet or drug.

Neurological Evaluation

Dr. Robert Soll:†

I would concur with Dr. Lee's statement that diabetes is very commonly complicated by severe arteriosclerosis. Not only is this true of coronary artery disease, but it is likewise true of all the vessels in the body, including the cerebral vessels. In diabetic neuropathy the most important etiological factor is probably an arteriosclerotic involvement of the vasa nervorum of the peripheral nerves, causing an inadequate vascular supply to the nerves, resulting in a *patchy demyelination* as well as loss of the axons themselves. Both motor and sensory conduction may be impaired. In an interesting review in

*See Test Your Word Score Page 1659.

**Medical Fellow Specialist and Instructor, Department of Medicine, University of Minnesota Hospitals.

†Neurologist, University of Minnesota Hospitals.

1957, Spratt and Hardin² noted that about 14% of all diabetics will develop a neuropathy. Neuropathies can involve all peripheral nerves, sensory and motor. Pain sensations are common and usually appear as burning paresthesias. Interestingly, some pains can be lightening-like, simulating those occurring in tabes dorsalis; this is called *diabetic pseudotabes*. Probably the most common peripheral nerve involved is the femoral, but the sciatic, median or ulnar nerve may also be implicated on occasion. A diabetic patient may develop a *foot drop*; frequently this may be associated with leg crossing, implicating pressure on the peroneal nerve. This suggests that a peripheral nerve in a diabetic patient may be more susceptible to trauma; however, some diabetics probably do not cross their legs and still get a foot drop.

Diabetic patients will frequently show an elevation of the cerebrospinal fluid protein, whereas patients who have no neurological symptoms will usually have a normal protein value. In a series of 84 cases of diabetic neuropathy, Bailey and Murray³ found a cerebrospinal fluid protein elevated above 50 mg.% in 73 patients, or approximately an 87% incidence.

Treatment

Treatment of diabetic neuropathy involves the same conservative principles as neuropathies in general: that is, good nursing care, bed rest, and relatively early passive range of motion to prevent contractures. Patients on prolonged bed rest frequently develop tightness in their calf muscles as a result of inactivity. Posterior splints of the lower legs and feet may also be used to support the feet in the correct posture during bed rest. Strict control of the caloric intake, together with very close regulation of insulin dosage, is an absolute necessity.

Very often patients with diabetic neuropathy do not respond well to treatment. There is no good explanation for this, however, since the definite cause of diabetic neuropathy is unknown, though arteriosclerotic changes may be responsible, and hyperglycemia may also be involved. Vitamins have been used to supplement the diet. Thiamine and vitamin B-12 are usually given, although these have not definitely been shown to be of specific help in diabetic neuropathy. Urinary tract infections as well as infections in other areas must be watched for and treated appropriately. Patients with neuropathies are prone to develop decubitus ulcers as well as trophic ulcers of the skin, which can be very painful but can be minimized with good nursing care. Symptomatically, some of the more troublesome problems in treatment of these patients are the burning paresthesias on the bottoms of their feet and the pains in their legs. These can be alleviated by the application of local heat, care being taken, however, not to burn the patient.

Psychological Evaluation

Dr. Manfred Meier:*

General intellectual functioning in this man is at a high average level; his full scale IQ on the Wechsler Adult Intelligence Scale was 116. His verbal IQ was 119, while his performance IQ was 110. This discrepancy of nine points is probably insignificant. In general, the subtest scatter does not support the notion that he has undergone any significant intellectual impairment. In order to confirm this inference, we gave a series of other tests covering a wide range of functions including planning with foresight ability as

*Associate Professor, Department of Neurology, University of Minnesota Hospitals.

measured by the Porteus Maze Test, immediate visual retention as measured by the Benton visual retention test, and the Bender visual-motor gestalt reproduction. Also some additional tests were given such as the Trail Making test and our new experimental measures including visual discrimination at a complex level of visual functioning and readaptation to rotated visual space. Throughout, there was no evidence of intellectual impairment, and therefore, by inference, no indication of organic cerebral dysfunction.

Personality

Personality functioning, however, shows some rather clear-cut abnormal indications on the Minnesota Multiphasic Personality Inventory in the form of deviations in a somatic, neurotic direction. He produces multiple elevations including high scores on the hypochondriasis, hysteria, psychopathic deviate and schizophrenia scale scores. The profile in general follows a downward slope characteristic of the somatic neuroses. There is a high probability that he generates multiple, diffuse, fluctuating somatic complaints which are likely to be referred to the periphery of the body but could include visceral complaints as well. Ordinarily such complaints, if generated on a somatic-neurotic basis, would be expected to help an individual achieve some measure of anxiety reduction or adaptation.

Anxiety

In this patient, secondary elevations on depression and psychasthenia suggest that such an anxiety or discomfort-reducing function has not been fully achieved. As a result we would infer that he has not been able to manage efficiently an anxiety-reducing adjustment on a conversion reaction basis. At this level of analysis one can never rule out organic considerations. In this situation, it can only be inferred that he is presenting evidence of considerable functional overlay. The most alarming aspect of his profile is that such high scores on the somatic neurotic scales are unusual in an individual of this age. Even in older individuals such scores are more often associated with a chronic conversion picture. At his age, I would even consider a vocational incapacitation on a neurotic basis as a potentially negative outcome; therefore I would strongly recommend that efforts be made to mobilize this individual at the earliest time through appropriate rehabilitation channels. Another alternative would be to consider psychotherapy as a treatment to modify what appears to be increasingly more dependent and maladaptive uses of somatization. However, chances are that he would reject psychogenic explanations and actively resist any efforts along these lines. Therefore, the clearest indications of behavioral abnormality in this array of data are the indications in the multiphasic of a chronic, somatic-neurotic adjustment, indications which I think, have implications for the immediate future as far as rehabilitation efforts are concerned. Whether or not he also has extensive medical problems with a clearly organic basis, I would not be surprised to find that some of his symptoms cannot be explained in organic terms. If we did successfully treat a medical condition to reduce certain complaints, one would predict that he would generate new complaints. Also he would probably generate even more dependence upon somatic complaints as a way of handling stress. I am somewhat alarmed by the data in terms of the prognostic implications they carry, and I would urge strongly that efforts be made to mobilize this man towards a more independent and productive kind of vocational and

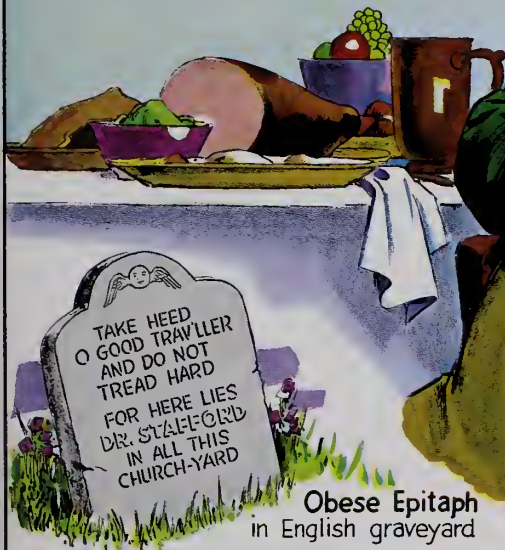
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interpersonal adjustment. I realize that this is a big order, considering the excessive extent to which he depends on somatic complaints, perhaps generating many of these to avoid work situations and other unpleasant interpersonal situations. In this instance, such mobilization may well become one of the more central aspects of any treatment program.

Social Evaluation

Miss Annie Laurie Baker:*

This interpretation is very interesting in respect to the social situation in which the patient now finds himself. He is a person with an easy, outgoing disposition. He speaks rather freely and is quite happy here.

Family Status

The patient comes from an interesting family. His father was a high school graduate and intended to enter law school; subsequently he spent two years at the University and then joined the police force. For some odd reason he is now a bartender. The patient is the oldest child in a family of five and the only boy. According to his wife, he has been very fond of his little sisters, but there seems to have been considerable rivalry. His mother is apparently a careless sort of person who paid very little attention to his medical problem when it arose.

The patient attended high school but did not graduate. I think it is very interesting that when he was beginning to have a hard time financially last March, he signed up for a correspondence course to finish high school. This cost him \$95 and he is still behind on those payments. Why he quit school is difficult to explain, particularly since he was within seven or eight credits of finishing. He was married at an early age. His wife, also not a high school graduate, is a very pleasant person. Their oldest child is now four. They have a second child 18 months of age, and their third child is expected in January.

Work Habits

Both the patient and his wife state that he has been a very hard worker. He has enjoyed salesmanship and been rather successful at it, although I notice that his work history reveals that he has had a great number of jobs in the past five years. In fact, in the short time they have been married (five years), they have had ten different addresses, purchased two homes and lost both of them. So there is more instability than you would expect to find in so young a person. His wife comes from a well-to-do family in which there are nine children; nevertheless, her father is paying on a \$3500 loan for the patient which amounts to \$144 a month. The patient and his family are now on village relief and have made application for Aid to Dependent Children. If this patient were going to be incapacitated for a period of two to three months, he would have to have some extra assistance, such as Aid to Disabled, which might only augment those tendencies brought out on the psychological report. While he is disabled he will be relieved of responsibility for himself and for his family. This will certainly interfere with his motivation. Even without assistance, he is largely dependent on his father-in-law. He says he has been a successful salesman, and his wife admits that he is an exceedingly hard worker. When he does work he puts in 16 hours a day; however, he has been ill much of the time. His last employment was selling appliances. He is

*Director Social Service Department, University of Minnesota Hospitals.

not concerned much about what he will do when he leaves here. Likewise, he seems to have little concern for his family; in the past when he has had trouble, he has simply gone home. His family has taken him in and never inquired about his wife. She expects her own family to help her out. So we have a young couple, soon to have their third child; he is 24 and she 22, with their whole future before them.

Vocational Rehabilitation Evaluation

Mr. Fred Borden:*

Dr. Meier has related the results of the Wechsler Adult Intelligence Scale test placing the patient in the high average ability range. During vocational counseling in the rehabilitation center we have observed him during the last week and have administered additional tests which would confirm the estimate of his general mental ability. On the other hand we have some other information which does not quite fit this picture.

Aptitude Tests

The State of Minnesota has a uniform testing procedure whereby each high school junior in the state is tested. This man was a junior in 1959 and his high school rank at that time was in the bottom 5% of the class. Further information includes the results of an achievement test, the Minnesota Scholastic Aptitude test which, with a high loading of word usage, is a good predictor of how a student might do in college and also necessarily reflects what he has learned in high school. In this test our patient scored better than just about 20 per cent of the high school juniors in Minnesota. A Co-op English test, which he also took at this time and which should reflect what he has learned in high school, also ranks him above 20 per cent of the Minnesota high school population. These measures of achievement are definitely not consistent with the measure of his intellectual ability we have obtained. We would expect that in a high school group he should rank probably around the seventy-fifth percentile if he were fully using his intellectual potential. I feel that the picture given to us by this data indicates that this patient under-achieved in high school, and this should help us understand why he dropped out. My information is that he left high school in his senior year, then tried to go back but got too slow a start and again quit. He began to work for the remainder of that year and transferred to another high school the next year. Following the same pattern as before, he dropped out during the first semester. School was not a satisfying experience for him. In discussing this, he commented, "Whenever I tried to study I just would think about all the fun my buddies were having and I'd have to get out and bounce around." He said that about 80% of his buddies were high school drop-outs. Thus the picture of his past high school academic achievement appears rather glib.

Vocational Aptitude

We have other information on more specific vocational aptitudes which is not nearly as discouraging. We gave him the battery of specific aptitude tests which are generally used in U. S. Employment Services, designed to measure specific aptitudes isolated from the general concept of intelligence. On none of these eight-part tests did he score significantly below average and, in two

*Vocational Counselor, Physical Medicine and Rehabilitation Department, University of Minnesota Hospitals.

areas, the results were quite good. For instance, he showed spatial ability in the strong average range; and his ability for clerical perception, which consists of rapid checking in order to identify errors or differences in written materials, would have to be considered above average—probably in the top 10% of the general population. He has taken two interest tests, the results of one of which are now available, showing an interest pattern consistent with his sales background, i.e., persuasive interest. These results are co-existent also with interest in the clerical computational area. In discussing his vocational plans, he says, "Well, this really is dependent on what the doctors tell me when I leave." This was his first reaction to my efforts to get him started thinking about his future in terms of jobs; he didn't feel that he could make any definite plans. On a second interview he said that one thing that interests him is drafting, also that he loves saleswork; which is consistent with his tested interest patterns. At the same time, he feels that control of his medical condition will probably necessitate at least an alteration in his selling job or perhaps a complete withdrawal from the selling area because of the lack of a routine schedule that often goes with it. I would suggest, in terms of his measured ability and aptitude, that the picture does not seem at all bleak from our standpoint; on the other hand, I have seen the results which Dr. Meier referred to in the multiphasic. My conclusion is that we should take all the immediate action we can to facilitate his contact with the world of work and with reality in general. I would be very much distressed to see him in a period of long passive convalescence. The desirable thing would be to get him active before this pattern becomes permanent.

What are the things that might be done from the vocational standpoint? Aside from the rather bleak prognosis psychologically, I would say that he has many good job assets, but I am a little disturbed about two conflicting pieces of data. Possibly Dr. Meier would comment on the elevation in scales one and three on the multiphasic, contrasting with the fact that he has been working 16 hours a day for a period of about a year, and also with the fact that he has had two selling jobs in which he was working from 8 a.m. to 10 p.m., six days a week. Specifically, I think that the Division of Vocational Rehabilitation of the State of Minnesota would be very willing to accept this man as a potential vocational rehabilitation case and might offer some kind of training program. An immediate consideration is: how can this man earn a high school diploma? One way would be to take the high school General Education Development test and be awarded a diploma by one of the high schools he attended. Also referral to the Division of Vocational Rehabilitation would be entirely appropriate in this case. I would like to continue to see him further, and when he leaves the hospital, I could make a referral to the Division of Vocational Rehabilitation.

Dr. Meier:

I did not want to imply that on the basis of something like the multiphasic alone, the prognosis should be considered bleak. I think there are a number of things working in this patient's favor: first, his substantial level of ability and secondly, his age. What alarmed me was the fact that profiles of this kind are unusual at this age level. Such a finding at this early age should serve to alert us to his present pattern of adjustment which, if allowed to become chronic, may definitely have negative implications from vocational and interpersonal standpoints. I do not know what the prognosis for a suc-

cessful work adjustment is for this case. I don't like what I see in the multiphasic, and if you press me to try to set a probability for his return to a successful work adjustment, assuming that he is already functioning at that level I could not do so. However, I think that his underachievement in high school is consistent with the multiphasic, as underachievement is typically associated with some personality disturbance, although there is no unitary personality disturbance that leads to underachievement. Ordinarily, in high school, underachievement is associated with character defects. In relation to the other things said about the multiphasic, I should have mentioned that there is evidence in this patient's profile of some character defects, in that he does not have a purely somatic neurotic code type. Rather, such features are probably intertwined with some passive aggressive traits, such as a tendency to manipulate and exploit others, poor judgment, and active avoidance of responsibility.

Dr. Soll:

I think this brings out very well the fact that illness carries with it innumerable problems above and beyond the medical ones. If we, as doctors, have the role of helping a patient return to a functioning level in society, we have a great task set out for us here. It is not simply a matter of controlling the diet and insulin.

The Following Recommendations Can Be Summarized:

1. Infectious processes should be frequently looked for by periodic checks of the patient's temperature, white blood cell count, chest x-rays, and dental examinations.
2. Strict control of the diabetes should be maintained through an adequate diet and precise regulation of the patient's insulin requirements.
3. Psychotherapy should be considered for the purpose of increasing the patient's understanding of his own problems as well as those of his family.
4. Vocational rehabilitation counseling should be continued with the ultimate aim of obtaining employment that will be compatible with the patient's physical and mental condition.
5. Financial support should be provided through Aid to Dependent Children until the patient becomes adequately self supporting.

Robert W. Soll, M.D., Chairman
Adult Community Services

Participating in the conference were: Miss Annie Laurie Baker, Director, Social Service Department; Miss Helen Kretchmer, Supervisor and Assistant Professor, Social Service Department; St. Dr. Steve Drosman; Dr. Richard Magraw, Director, Comprehensive Clinic Program; Dr. John Brantner, Associate Professor, Clinical Psychology Department; Dr. Manfred Meier, Associate Professor, Department of Neurology; Dr. Gerald Lee, Medical Fellow Specialist and Instructor, Department of Medicine; Mr. Fred Borden, Vocational Counselor, Physical Medicine and Rehabilitation Department; Mr. Jerald Forster, Instructor, Physical Medicine and Rehabilitation Department and Dr. Robert W. Soll, Neurologist.

References

1. Williams, R. H., *Ann Intern Med* 63:3, 1965.
2. Spratt, I. L., and Hardin, R. C., *J Iowa Med Soc* 47:571, 1957.
3. Bailey, C. C., and Murray, J., *The Nervous System In Diabetes*. In: Joslin, E. P., Root, H. F., White, P., Marble, A., and Bailey, C. C.: *The Treatment of Diabetes Mellitus*. Philadelphia, Lea and Febiger, 1948.

Two Views

You can have the guy who's always searching for the bright side; I'll take the one who's in there polishing up the dull.

Don Marshall, Partners



Clinical Path Conference

Respirator Lung Syndrome

Robert L. Strom, M.D.:*

A 35-year-old white housewife was hospitalized with a complaint of left flank pain of three days' duration. The pain was described as steady with some radiation to the left inguinal region. Fever and chills were noted on the day of admission.

Diabetes mellitus had been present for 30 years. An insulin dosage of 37 units nph had been maintained; however, increased glycosuria had been present for the past week. The patient had been hospitalized on nine previous occasions for pyelonephritis over a 20-year period.

On examination, the blood pressure was 100/70, the pulse 90 per minute, the temperature 102.2°F., and the respirations 24 per minute. The patient was pleasant and cooperative and did not appear ill. Some tenderness was elicited in the left costophrenic angle.

On the evening of the first hospital day, intravenous 50% dextrose was required to maintain the blood sugar above 50 mg.%. A chest X ray was interpreted as normal. A flat plate of the abdomen showed a large ureteral stone at the left ureterocystic junction. An emergency intravenous pyelogram showed nonfunction of the left kidney and some hydro-nephrosis on the right. Treatment consisted of intravenous fluids, Colymycin and nasogastric suction. Intermittent doses of Aramine were required to maintain a systolic blood pressure greater than 90 mm. of mercury.

On the second hospital day, a left nephrectomy and partial ureterectomy was performed. During induction of anesthesia, the systolic blood pressure fell to sixty mm. of mercury but responded to intravenous fluids and a reduction of the amount of Halophane administered.

After surgery, the patient remained in the post-anesthetic recovery room for the first two postoperative days because of weak and inadequate respirations. She was totally dependent upon a Bird Mark 7 respirator and a nasotracheal tube. On the first postoperative day, she developed signs of congestive heart failure and was digitalized. Several attempts to stop respiratory assistance resulted in hypoventilation and cyanosis. A chest X ray showed bilateral symmetrical consolidation of the mid- and lower lung fields. On the second postoperative day, a tracheotomy was performed. A blood culture grew out *Proteus* species and the antibiotic therapy was changed to intravenous Keflin.

On the third postoperative day, the patient developed marked dyspnea and cyanosis. The lungs revealed diffuse small rales and scattered wheezes. An electrocardiogram showed an acute right ventricular strain pattern. Right calf tenderness was present but there was no edema of the extremities. Heparin and dextran were administered because of suspected thrombophlebitis. A urine culture grew out *Proteus* species. Thereafter, the patient's condition remained unchanged, although respiratory assistance continued to be necessary.

On the sixth postoperative day, regular insulin was given because of moderate diabetic acidosis. A few hours later, cardiac arrest occurred during tracheal suction, and resuscitation attempts were unsuccessful. Vital signs, intake and output, and laboratory data during hospitalization are listed in Table I.

*Associate Pathologist, Hennepin County General Hospital

TABLE I

Hospital Day	1	2	3	4	5	6	7	8
Temp.	103 ²	102		101	100 ¹	100 ²	99 ⁸	99 ⁶
Pulse	124	110		130	150	115	120	40
B.P.	108	90			110	110	120	
	60	50			55	60	70	
Intake	4800	4490	2810	3400	3320	3550	3920	
Output	845	2130	3095	2245	1656	2480	3325	
Resp.	24	26		40	38	35	40	
Hgb.	14.6	12.5			11.4	9.2	9.2	
Wbc.	16,000	22,200			16,700		17,300	
Urine								
Sugar	3+	4+						
Acetone	Pos	3+						
Wbc.	125	95						
RBC	4	Occ.						
BUN	20	21				16	17	
Sugar	293	315			279		40	
CO ₂	17.5	18			15	22	20	
pH					7.35	7.38		7.16
P _i O ₂						40		
P _i CO ₂						46		

Clinical Discussion

Dr. Thomas Mulrooney:*

This young diabetic woman's presenting symptoms strongly suggested a renal stone and recurrent pyelonephritis. Her insulin requirements of 37 units of NpH per day is not unusual for a juvenile diabetic. Apparently, her initial chest X ray was normal. She was alert and cooperative with only mild left costovertebral angle tenderness. On the evening of her first hospital day, 50% dextrose had to be given intravenously in order to keep her blood sugar over 50 mg.%. This disturbed me considerably at first until Dr. Gerald Onstad explained that the lady had received regular insulin earlier in the day and apparently had not been eating adequately. The observed hypotension was apparently due to gram-negative sepsis since we have later laboratory confirmation of *Proteus* organisms in the blood. On the second hospital day, she underwent a left nephrectomy and partial ureterectomy.

Then we come to the first part of her course that is peculiar. She remained in the postoperative recovery room for the first two post-surgical days because of weak, inadequate respirations. During this time, she was totally dependent on a Bird respirator and a nasotracheal tube. In addition, she developed signs of congestive heart failure and was digitalized. Subsequently, all attempts to stop respiratory assistance failed since she promptly developed hypoventilation and cyanosis. Somewhere about this time, she had a tracheotomy. This was probably done since a nasotracheal tube cannot be left in place longer than 48 hours because of danger of erosion of the vocal cords. On the third postoperative day, she developed marked dyspnea associated with a right ventricular strain pattern on her electrocardiogram. With the presence of right-calf tenderness, it is not surprising that it was felt that she was developing pulmonary emboli.

*Attending physician, Department of Internal Medicine, Hennepin County General Hospital.

Tracheal Suction and Sudden Death

On the sixth hospital day, during tracheal suction, a cardiac arrest occurred and all resuscitation attempts were unsuccessful. Sudden death is a potential hazard of tracheal suction. During the time the patient is suctioned, the oxygen source over the tracheal tube has to be removed and when suction is applied over the airway, the patient abruptly becomes very severely hypoxic. Investigators have made measurements with an ear oximeter during tracheal suction and have demonstrated a dramatic fall in oxygen tension during suction. For this reason, we recommend that when tracheal suction is carried out, each suction attempt be kept to a very short period of not over 10 to 15 seconds. Then the oxygen source can be replaced over the trachea and the patient can be ventilated once again prior to the next suction attempt. It seems likely that even with these precautions this patient became sufficiently hypoxic to suffer a cardiac arrest. The reason she became so severely hypoxic, however, is part of the primary lung problem which eventually led to her death. Now I wonder if we could review the X rays with Dr. Tsai?

Dr. S. H. Tsai:*

In reviewing this diabetic lady's films, we discovered that she had quite extensive papillary necrosis on her intravenous pyelogram as early as 1953, twelve years prior to admission. This is not the fatal fulminating course of papillary necrosis, but early deformities in the papillae were present in the left kidney and also to some extent in the right kidney. The initial chest X ray on this admission was within normal limits (Figure 1). On the chest

*Chief, Department of Radiology, Hennepin County General Hospital.



Fig. 1—Normal admission chest roentgenogram.

film taken on the first postoperative day, a small pneumothorax is seen on the left side and there are extensive infiltrations in both lung fields. By the second postoperative day, she has a more extensive alveolar infiltration which is more or less symmetrical (Figure 2). Between the second and third days there is further progression and, thereafter, the chest findings remain unchanged. The X-ray interpretation at that time was diffuse pulmonary edema. In making the diagnosis, we realized that the cardiac silhouette was not enlarged and there was very little change over several days' observation. This is somewhat unusual for pulmonary edema; most often the infiltration shifts and varies from one day to another rather than remaining totally confluent.



Fig. 2—Dense bilateral alveolar infiltration occurring postoperatively.

Dr. Mulrooney:

The part of this lady's course which is unusual and holds our major interest is the difficulty encountered in weaning her off the mechanical respirator. On the third postoperative day, she developed further respiratory difficulty and the possibility of pulmonary emboli was entertained. One could hardly refute this diagnosis.

Blood Gas Measurements

On the fourth hospital day, the arterial blood gas measurements were made, and I might now call your attention to Table 1 of the protocol. The first thing to notice is that the patient was somewhat tachypneic when she entered the hospital, but her respiratory rate progressively rose and by the fourth hospital day was 40 per minute. On the sixth postoperative day, the arterial

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DECLOMYCIN Demethylchlortetracycline should be equally or more effective therapeutically than other tetracyclines when the offending organisms are tetracycline-sensitive.

Contraindication: History of hypersensitivity to demethylchlortetracycline.

Warning—In renal impairment, usual doses may lead to excessive accumulation and liver toxicity. Under such conditions, lower than usual doses are indicated, and, if therapy is prolonged, serum level determinations may be advisable. A photodynamic reaction to natural or artificial sunlight has been observed. Small amounts of drug and short exposure may produce an exaggerated sunburn reaction which may range from erythema to severe skin manifestations. In a smaller proportion, photoallergic reactions have been reported. Patients should avoid direct exposure to sunlight and discontinue drug at the first evidence of skin discomfort. Necessary subsequent courses of treatment with tetracyclines should be carefully observed.

Precautions—Overgrowth of nonsusceptible organisms may occur. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects—Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes. A rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose related. Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth—dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs discontinue medication and institute appropriate therapy.

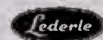
Average Adult Daily Dosage: 150 mg q.i.d. or 300 mg b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

In the treatment of syphilis a dosage schedule of a total of 12 to 18 Gm. given in equally divided doses over a period of 10 to 15 days should be followed. Close follow-up observation of the patient is recommended, including appropriate laboratory tests, since demethylchlortetracycline has not had adequate evaluation in all stages of syphilis. Spinal fluid examination should be included as part of this follow-up.

Acute gonococcal anterior urethritis in males has been treated effectively with a single dose of 600-900 mg. of DECLOMYCIN Demethylchlortetracycline. Individuals unable to tolerate large single doses due to gastrointestinal side effects may be treated with 150 mg. every 6 hours for a minimum of 4 doses or 300 mg. every 12 hours for a minimum of 2 doses. Females should be treated with a dosage of 150 mg. every 6 hours or 300 mg. every 12 hours until a cure is effected.

Primary Atypical Pneumonia (Eaton Agent): The average adult daily dosage is 900 mg. in 3 divided doses for six days.

LEDERLE LABORATORIES, A Division of
American Cyanamid Company, Pearl River, N.Y.



blood gas studies were strikingly abnormal, particularly if they were drawn while the patient was on the respirator. I direct your attention to the PO_2 of 40 and the pCO_2 of 46 mm. of mercury. The normal CO_2 tension in blood is 40 mm. of mercury with a little room for variation, but 46 mm. of mercury is definitely elevated. It is not an extreme elevation, but it means that this patient, at that particular time, was having difficulty eliminating CO_2 . Even more dramatic is the PO_2 of 40 while the patient is on a respirator. The normal PO_2 when one breathes room air is 90 mm. of mercury. A patient who is on a respirator is inhaling enriched oxygen concentrations, and the alveolar oxygen tension may be several hundred millimeters of mercury, depending upon how the respirator is set up and what concentration of oxygen is being used. The difference then between the oxygen tension in the alveolar air and the oxygen tension in the arterial blood of this patient must have been enormous. This represents a major shunt; for some reason, large amounts of blood were bypassing the ventilated portions of the lung.

What we have to discuss then in this patient is what sort of problem caused us to be unable to remove her from a respirator. Why should a person develop persistent hypoventilation after the respirator is removed?

Chronic Lung Disease

The first thing one thinks of is the presence of chronic lung disease. In patients with obstructive emphysema and severe underlying chronic pulmonary disease, when we attempt to remove the respirator the patient is unable to ventilate for himself sufficiently. One must consider depression of the respiratory center by the administration of oxygen. This situation almost invariably occurs in patients who before oxygen was administered were seriously hypoventilated and had high concentrations of arterial CO_2 . Under these conditions, the respiratory center is depressed by the continuous excessive amount of CO_2 present. We assume that the low oxygen tension acts as a stimulus to respiration and when we relieve this by administering oxygen the patient gets into trouble. We can readily dismiss this in the patient under discussion since the initial chest X ray was perfectly normal and there was nothing in the history or physical examination which would suggest chronic lung disease. We evidently started out with a patient with normal lungs.

Central Nervous System Disease

A massive cerebral vascular accident such as a sudden destructive lesion of the brain stem can cause such a respiratory disturbance. Nothing in the protocol suggests this patient developed any other neurologic abnormalities; so this seems highly unlikely.

Diseases of the Chest Wall

Leaving the nervous system, one could think of diseases that affect the chest wall or its innervation and make it impossible for the patient to ventilate normally. Examples of these abnormalities would be a patient who has a traumatic flail chest or some restrictive disease of the chest wall such as kyphoscoliosis or rheumatoid spondylitis. A patient who has poliomyelitis may fall into this category, but none of these conditions appear to apply to our patient.

Neuromuscular Paralysis

We might consider some weakness of the respiratory muscles due to a toxin or poison such as in tetanus, hypokalemic paralysis, or an inherited deficiency of the enzyme pseudocholinesterase. In the general population there are a few people who do not have a normal amount of pseudocholinesterase and are discovered following surgical anesthesia. There have now been some case reports of difficulties encountered with patients who were given succinyl choline, an agent which paralyzes the muscles and is usually destroyed in about three or four minutes by pseudocholinesterase. When given to these patients, the succinyl choline is not destroyed for hours and hours and the patients require prolonged respiratory assistance. As nearly as I can determine, in this syndrome the entire duration of the problem is not longer than four or five hours and succinyl choline paralysis seems quite unlikely in our patient.

So we are finally left with the problem of a patient who was able to breathe normally prior to her surgery but never afterward, and we are forced to conclude that some sort of change in her lung developed during the time that she was on the respirator. This conclusion is certainly strengthened by the X rays, with their progression from a normal chest to a grossly abnormal picture (Figure 2).

Pulmonary Edema

One of the diagnostic possibilities that was raised was pulmonary edema, and I think that in a sense she did have pulmonary edema although not from left-sided heart failure which we usually consider to be the cause of that state. Her heart was not enlarged and digitalization and positive pressure breathing did not alter the picture.

Pneumonia

Another possibility we would have to consider is that she may have developed a massive infection in the lung, presumably due to *Proteus* organisms. I guess we cannot entirely exclude that event, but she failed to respond to antibiotics and the infiltration remained unchanged.

Insufficient Inflation of the Lung

That leaves us with two different possibilities that can occur to individuals who are ventilated with respirators. These two conditions may be related to each other. The first one I want to mention is the effect of insufficient inflation of the lung. As you are well aware, everyone sighs from time to time (women perhaps more often than men). Each individual takes a deep breath on the average of four or five times an hour. It has been demonstrated in animals and human beings that this sighing serves a very useful purpose. In fact, if an animal or human being is ventilated with a constant tidal volume and is not permitted to sigh, he will get into respiratory difficulty. This difficulty is manifested by a progressive fall in the arterial oxygen tension and a progressive decrease in the pulmonary compliance or distensibility of the lung. A physiologist in Boston, Jere Meade, first demonstrated this in dogs, and he interpreted the data to indicate the development of progressive microatelectasis.¹ In a normal lung, when expiration occurs, some of the small air

spaces collapse, but expand again with the next breath. His contention was that some of them did not re-expand and were only expanded when a deeper breath or sigh occurred. Bendixon, who is in charge of a large respiratory unit in Boston, made some physiological measurements in anesthetized human beings to demonstrate this same phenomenon.^{2,3}

This might have occurred with our patient and demonstrates that when anyone is put on continuous artificial ventilation, the attending physician should instruct personnel to see to it that the patient takes at least one deep inspiration every 15 minutes. This can be done in an unconscious patient simply by increasing the pressure on the respirator. Otherwise, the arterial oxygen tension will progressively fall even though the patient is being ventilated with 100% oxygen. Eventually, the amount of pressure required to inflate the lungs will rise even to a point that cannot be achieved.

Respirator Lung Syndrome

The other problem that can occur with people on respirators has been called "respirator lung syndrome" and may be a manifestation of oxygen toxicity. Recently, Cederberg in Sweden and Nash in Boston have reported pathological changes in patients who are ventilated with high oxygen concentrations over a prolonged period of time.^{4,5} Nash compared the lungs of 70 respirator patients who died in a respiratory care unit with the lungs of 70 other people who died elsewhere in the same hospital. Both the controls and the respirator patients had some findings in common, such as bronchopneumonia, pulmonary infarction, pulmonary edema and congestion. However, there were some pathologic changes that were confined almost exclusively to patients who had been on a respirator. In those who died rather early this consisted primarily of edema of the alveolar septae with hyaline membranes similar to membranes seen in respiratory distress syndrome of the newborn. Those patients who died after a longer period on the respirator showed a proliferative response in the alveolar septae.

These investigators attempted to correlate these pathological changes with what had been done to the patients during life. They divided the patients into four groups. Group I included those who had received positive pressure for less than ten days with relatively low concentrations of oxygen (40 to 90%). Group II were those who received respiratory assistance for greater than ten days with the same low concentration of oxygen. Group III were those who received assistance for less than ten days but inhaled 100% oxygen. Group IV were ventilated for greater than ten days with 100% oxygen. In brief, they found that the pathological alterations increased the longer the patients were on the respirator and with higher concentrations of oxygen inhaled. They also found that if they ignored the oxygen concentration and just compared the changes on the basis of time on the respirator, there was no difference in the two groups. It was their opinion that the damage resulted from the oxygen administration.

Oxygen Toxicity

These workers pointed out something that startled me. The oxygen concentration delivered by the commonly used positive pressure respirator when the main stream nebulizer is running (and this is the usual mode of operation) is about 90%. This was surprising because the literature that comes with the machines states that when the machines are set for "air mix" they deliver an

oxygen concentration of about 40%. I always thought this was true and never measured it. In a sense, it is true, but the problem is that the machines in practice are always set up with a heated nebulizer powered with 100% oxygen. What the patient breathes is a mixture of air coming out of the machine and 100% oxygen coming out of the nebulizer resulting in an inhaled oxygen concentration of about 90%.

It has been demonstrated in the past that oxygen in high concentration is toxic to both animals and man. Dogs who breathe 100% oxygen at atmospheric pressure die in about three days, and human beings who breathe 100% oxygen at atmospheric pressure develop symptoms of chest pain, cough and diminished pulmonary compliance which are thought to be at least partly due to oxygen. In any event, there is accumulating evidence that high oxygen tensions could be potentially toxic when given for a long period of time.

It should be said at the same time, however, that these high oxygen tensions may be necessary. It is certainly apparent that this lady could not have survived without the high oxygen tension since her arterial PO_2 was only 40 mm. of mercury, barely enough to sustain life. I certainly do not want to leave the impression that cyanotic patients should not be given oxygen because it might hurt them. This appears to be a threat that we must accept at present, and hopefully we may find some solution for it.

My conclusion then would be that the cause of death in this patient was progressive respiratory failure secondary to the use of a mechanical respirator with relatively high oxygen tension and that in addition she had diabetes mellitus, pyelonephritis, and acute *Proteus* septicemia.

Clinical Diagnosis:

1. Respirator lung syndrome with oxygen toxicity and hyaline membrane disease.
2. Diabetes mellitus.
3. Ureteral lithiasis and acute pyelonephritis.
4. Septicemia due to *Proteus* species.

Pathological Findings

Dr. Robert L. Strom:*

The autopsy findings in this lady involved many systems, and I will take up last the findings in the lungs which hold the major interest. The pleural cavities contained 500 and 700 cc. respectively of pink-colored fluid.

Bacterial Endocarditis

The total heart weight was only 300 grams and the heart appeared normal to external examination. When the heart was opened the valves were examined and multiple vegetations were seen on the aortic and tricuspid valves. The aortic valve was not perforated due to the infection, but one can see a jet lesion on the intima of the aorta above the valve in Figure 3. This represents good evidence of acute bacterial endocarditis since *Proteus* septicemia occurred during life. When we examined the tricuspid valve we again found evidence of right-sided bacterial vegetations with several of the valve leaflets being involved (Figure 4). The vegetations were made up primarily of layered platelets with many neutrophils and histiocytes confirming an infectious etiology. The absence of stainable organisms is not surprising since the patient was on Keflin and this antibiotic is known to be highly effective against

*Associate Pathologist, Hennepin County General Hospital.

Proteus species. The patient had evidence of diffuse embolic phenomena involving the brain, spleen and kidney.

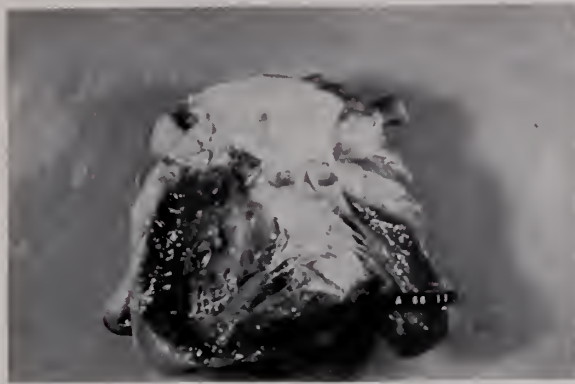


Fig. 3—Heart showing acute bacterial endocarditis of aortic valve. Jet lesions are noted on the intima of the aorta and on the aortic leaf of the mitral valve.



Fig. 4—Tricuspid valve with verrucous vegetation from right-sided acute bacterial endocarditis.

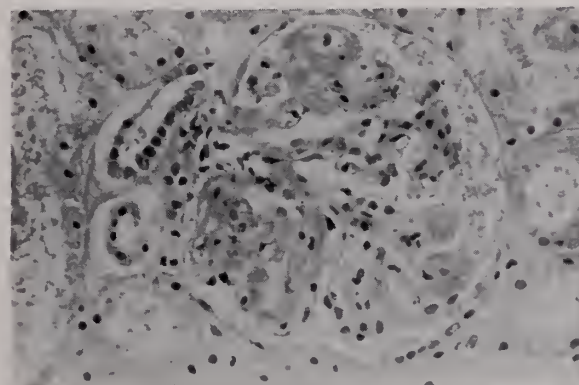


Fig. 5—Renal glomerulus showing nodular glomerulosclerosis of Kimmelstiel Wilson $\times 400$.

Renal Findings

A number of findings were observed in the lower urinary tract. There was a large calculus in the left ureter and the left kidney had been removed. The right kidney was not obstructed by a ureteral calculus, but it did show some papillary necrosis and evidence of acute pyelonephritis. It also showed thinning of the renal cortex down to about 3 mm., suggesting chronic renal disease with superimposed pyelonephritis. A few small microabscesses

were seen in the renal substance, and the glomeruli showed changes of a nodular type characteristic of Kimmelstiel-Wilson's disease (Figure 5). Several glomeruli in the kidney showed evidence of focal embolic nephritis with infarction of portions of the glomerulus and infiltrations of neutrophils (Figure 6). Therefore, we feel the kidney was the source of the *Proteus* septicemia, which may have resulted in the infection of a normal aortic and tricuspid valve.

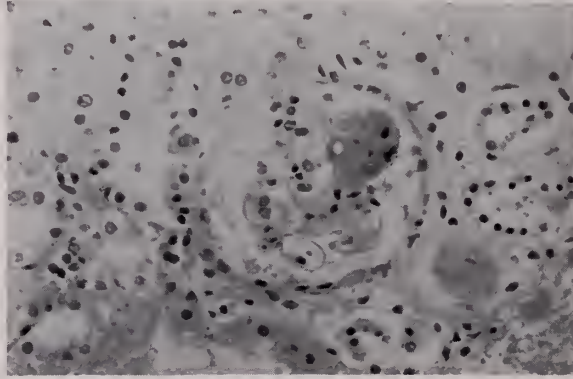


Fig. 6—Focal infarction of renal glomerulus by a bacterial embolus $\times 100$.

Oxygen Alveolopathy

The lung findings were extremely interesting. The lung weights were 1100 and 1150 grams respectively, making a combined weight of 2250 grams. In the studies of Nash, the combined lung weights in histories of 70 patients nearly all exceeded 1800 grams. A striking thing about these lungs is that they stand up firmly and do not collapse as a normal lung would when you place it on a table. The cut surface of the lung is fleshy and meaty, and as we cut into the lung, no fluid comes forth from the cut surface (Figure 7). A small hemorrhagic pulmonary infarction is present at the left apex of the lung.



Fig. 7—Heavy gross lung with fleshy fibrinous cut surface.

Histologic sections of the lung confirm the clinical impression of oxygen toxicity. Nash divided the pathologic response into two phases. The initial phase was termed exudative and consisted of disruption of alveolar capillaries with hemorrhage into alveolar spaces, edema of the interalveolar septae and development of a fibrin membrane. The second or proliferative phase was characterized by a fibroblastic reaction with resulting thickening of the

alveolar septae. In Figure 8 we see well-developed alveolar membranes which tend to line the alveolar spaces. In addition, one can see increased macrophage activity. It has been felt that the alveolar macrophages may be inactivated by oxygen since they produce surfactant, a lipoprotein which tends to restore the normal amount of lubrication to the alveoli so that they can open up and be aerated.

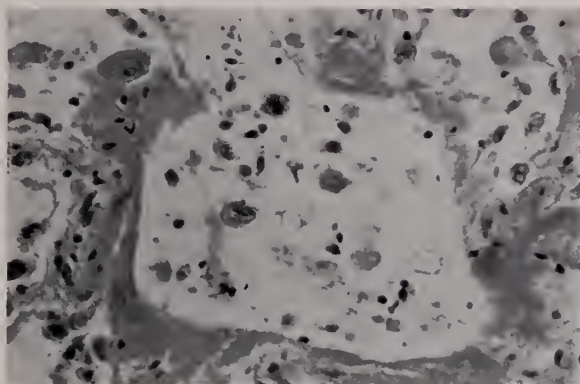


Fig. 8—Fibrin membrane surrounding alveolar with increased macrophage activity $\times 400$.

With the Bird Mark 7 and the Bennett PR 1 respirator, the nebulizer flow rate may be 6 to 8 liters per minute, and with the use of oxygen to power the nebulizer, the air mixture delivered contains 93% oxygen. With compressed air used to power the nebulizer, the air mixture contains 60% oxygen. In this institution we use a Bird Mark 7 respirator routinely. Since the pathologic findings described by Nash correlated well with the high oxygen tension but did not correlate with the length of time on the respirator, we may be dealing with a misnomer. The disease state in the lung should not in the strictest sense be interpreted as a respirator lung but rather an oxygen alveolopathy. It has been proposed that the inspired oxygen concentration of respirator patients be monitored and that high oxygen tensions be lowered as soon as feasible.

Pathological Diagnosis

1. Respirator lung syndrome (oxygen alveolopathy with fibrin membranes of the lung).
2. Diabetes mellitus (clinical).
3. Ureterolithiasis with acute pyelonephritis and *Proteus* septicemia.
4. Acute bacterial endocarditis of the aortic and tricuspid valve with systemic embolization.
5. Nodular glomerulosclerosis of the kidney (Kimmelstiel-Wilson disease).

Robert L. Strom, M.D.
Hennepin County General Hospital

References

1. Meade, J., and Collier, C.: Relationship of the Volume History of Lungs to Respiratory Mechanics in Anesthetized Dogs. *J Appl Physiol* 14:669, 1959.
 2. Bendixen, H. H., et al.: Impaired Oxygenation in Surgical Patients During General Anesthesia with Controlled Ventilation. A Concept of Atelectasis. *New Engl J Med* 269:991, 1963.
- 3-5 May be secured from the author or the reprints.

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Use Enduron as an ideal starting therapy in mild hypertension. Use it too, as a basic therapeutic building block with which other agents can be joined, for managing your more resistant hypertensives.

Once a day, every day

ENDURON[®]
METHYCLOTHIAZIDE



DAILY
DOSAGE
RANGE

Minimum



2.5 mg. tablet

Usual



5 mg. tablet

Intermediate



7.5 mg.

Maximum



10 mg.

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To build added response, shift to Enduronyl



The deserpidine component adds enhanced antihypertensive activity

The rauwolfia component of Enduronyl is deserpidine (Harmony[®]), a purified crystalline alkaloid supplied only by Abbott. It augments Enduron with its own antihypertensive and tranquilizing action.

Thus the combined clinical effect of these two therapeutic building blocks in Enduronyl is greater than can ordinarily be achieved with either alone.

To add flexibility, Enduronyl comes in two strengths: regular and Forte. Both provide 5 mg. of Enduron. The variation is where most helpful: in the deserpidine. The tablets are scored, and give a surprisingly wide and economical choice of once-a-day doses (see below).

Choose Enduronyl for your patients in the broad range of mild to moderate hypertension. Patient acceptance is excellent!

Once a day, every day

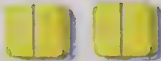
ENDURONYL[®]

METHYLOTHIAZIDE 5 MG. WITH DESERPIDINE 0.25 MG.

ENDURONYL FORTE

METHYLOTHIAZIDE 5 MG. WITH DESERPIDINE 0.5 MG.



	Minimum	Usual	Intermediate	Maximum
DAILY DOSAGE RANGE	 2.5 mg. methyclothiazide 0.125 mg. deserpidine	 5 mg. methyclothiazide 0.25 mg. deserpidine	 7.5 mg. methyclothiazide 0.375 mg. deserpidine	 10 mg. methyclothiazide 0.5 mg. deserpidine
DAILY DOSAGE RANGE	 2.5 mg. methyclothiazide 0.25 mg. deserpidine	 5 mg. methyclothiazide 0.5 mg. deserpidine	 7.5 mg. methyclothiazide 0.75 mg. deserpidine	 10 mg. methyclothiazide 1 mg. deserpidine

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Eutonyl affords a different kind of basic therapy for moderate to severe cases



Effect tied to reduced peripheral vascular resistance; no central depressant action

Eutonyl is a unique nonhydrazine agent. It is reported to act by reducing peripheral vascular resistance.^{1,2}

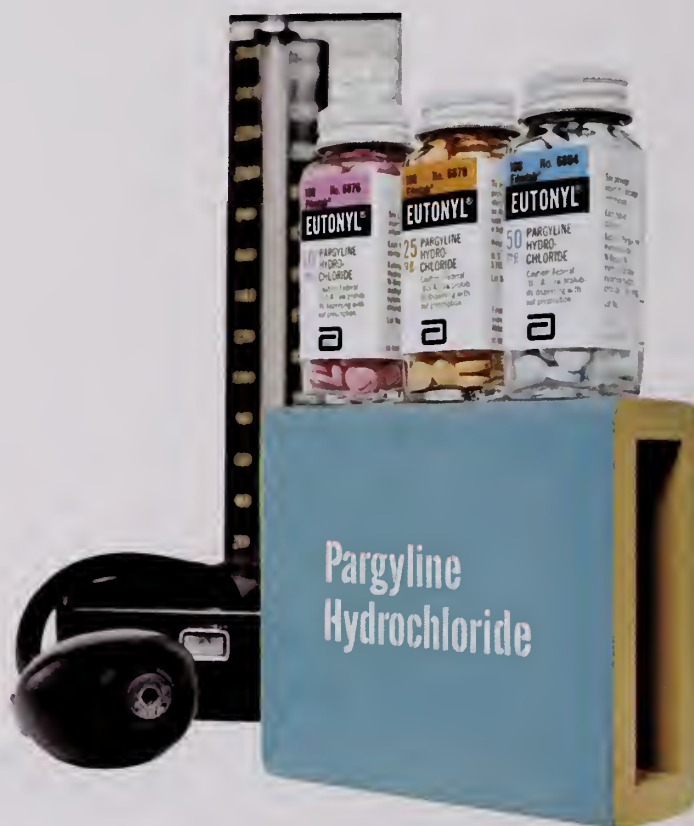
In clinical trials, significant reductions in mean blood pressure were seen in 84% of patients studied—all were moderate to severe cases. Eutonyl lowers diastolic in proportion to systolic, and in about half of the cases studied, reductions in the sitting and recumbent positions were nearly as great as in the standing position.

Most important: There is no central depressant action. In fact, some patients reported an *increased* sense of well being.

Here, then, is a highly effective *basic treatment* for moderate to severe cases—and one that will not hamper your patient with lethargy or drowsiness while on treatment.

Once a day, every day

EUTONYL®
PARGYLINE HYDROCHLORIDE



DAILY DOSAGE RANGE	Minimum	Usual starting	Intermediate	Maximum
	 10 mg. tablet	 25 mg. tablet	 50 mg. tablet or as needed	 200 mg.

1. Brest, A. N., et al., Cardiac and Renal Hemodynamic Response to Pargyline, *Ann. N. Y. Acad. Sci.*, 107-1016, 1963.

2. Winsor, T., Pargyline Hydrochloride, Hypertension, Urinary Tryptamine, and Vascular Reflexes, *Geriatrics*, 19:598, Aug., 1964.

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Eutron adds thiazide for enhanced therapy with milder side effects



Only a 7/4 mm. span between standing and recumbent pressures in clinical trials—reduced chance of orthostatic hypotension

The combining of Eutonyl and Enduron in Eutron permits a significantly greater antihypertensive effect than with either agent used alone. This in turn may allow therapeutic success with lesser dosage—and correspondingly milder side effects.

A significant finding in clinical trials was the drug's action in lowering blood pressure to *nearly equal levels in all body positions*. Total average spread between standing and recumbent readings (after treatment) was only 7/4 mm. Hg.

Thus, in your moderate to severe cases, Eutron affords a usually smooth course of therapy, often with reduced likelihood of orthostatic effects. (The usual precautions against rising suddenly, of course, will always apply.) And, because of the thiazide component, Eutron may be used in the presence of congestive heart failure.

Once a day, every day

EUTRON™

PARGYLINE HYDROCHLORIDE 25 MG.
WITH METHYCHLOTHIAZIDE 5 MG.



DAILY DOSAGE RANGE

Minimum



12.5 mg. pargyline hydrochloride and 2.5 mg. methyclothiazide

Usual starting



25 mg. pargyline hydrochloride and 5 mg. methyclothiazide

Intermediate



37.5 mg. pargyline hydrochloride and 7.5 mg. methyclothiazide

Maximum



50 mg. pargyline hydrochloride and 10 mg. methyclothiazide

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ENDURON[®] | ENDURONYL[®]

METHYLCLOTHIAZIDE

Each tablet contains
Methyclothiazide 5 mg. with
Deserpidine 0.25 mg. or 0.5 mg.

Indications: Enduron is used to control edema and mild to moderate hypertension; also used with other drugs for hypertension. Enduronyl is used in mild to moderately severe hypertension; when used with Enduronyl, more potent agents can be given at reduced dosage to minimize undesirable side effects.

Contraindications: Neither Enduron nor Enduronyl should be used in severe renal disease (except nephrosis) or shutdown; in severe hepatic disease or impending hepatic coma; in patients sensitive to thiazides. Hepatic coma has been reported as a result of hypokalemia in patients receiving thiazides.

Enduronyl is contraindicated in patients with severe mental depression and suicidal tendencies, active peptic ulcer, or ulcerative colitis.

Warnings: Consider possible sensitivity reactions in patients with a history of allergy or asthma. If added potassium intake is indicated, dietary supplementation is recommended. Enteric-coated potassium tablets should be reserved for cautious use only when adequate dietary supplementation is not practical because those tablets may induce serious or fatal small bowel lesions consisting of stenosis with or without ulceration. These small bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs.

Precautions: Use thiazides with caution in severe renal dysfunction, impaired hepatic function, or progressive liver disease. In surgical patients, thiazides may reduce the response to vasopressors and increase the response to tubocurarine. Use thiazides with caution in pregnancy (bone marrow depression, thrombocytopenia, or altered carbohydrate metabolism have been reported in certain newborn infants). Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. Antihypertensive response may be enhanced following sympathectomy.

Use Enduronyl with caution in patients with a history of peptic ulcer, as rauwolfias may increase gastric secretion. Discontinue at the first sign of mental depression. Rauwolfia alkaloids may increase hypotensive effects of surgery or anesthesia, and should be discontinued two weeks prior. They also lower the convulsive threshold and shorten seizure latency. In epilepsy, dosage adjustment of anticonvulsant medication may be necessary. Alcohol, barbiturates, or narcotics may potentiate action of deserpidine.

Adverse Reactions: During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). All patients should be observed for signs of hyponatremia ("low-salt" syndrome). Reported thiazide reactions include: anorexia, nausea, vomiting, diarrhea, headache, skin rash, dizziness, paresthesia, weakness, photosensitivity, jaundice, and pancreatitis.

Reported rauwolfia reactions include: nasal stuffiness, nausea, weight gain, diarrhea, aggravation of peptic ulcer, epistaxis, skin eruption, and reduction of libido and potency. Excessive drowsiness, fatigue, weakness, and nightmares may signal early signs of mental depression.

EUTONYL[®] | EUTRON[™]

PARGYLINE HYDROCHLORIDE

Each tablet contains
Pargyline Hydrochloride 25 mg.
with Methyclothiazide 5 mg.

Indications: For treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. Not recommended for patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone. It is desirable to establish the dosage of Eutron by administering component drugs separately.

Contraindications: Pheochromocytoma, advanced renal disease, increasing renal dysfunction, paranoid schizophrenia and hyperthyroidism. Hepatic coma has been reported as consequence of hypokalemia with thiazide therapy. Until further experience is gained not recommended for patients with malignant hypertension, children under 12, or pregnant patients.

Concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyl dopa. 2 week interval should separate therapy and use of these agents.

Methyclothiazide is contraindicated in patients with known sensitivity to thiazides.

Warnings: Pargyline hydrochloride is a monoamine oxidase inhibitor. Warn patients against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When indicated, alcohol, narcotics (meperidine should be avoided), antihistamines, barbiturates, chloral hydrate, and other hypnotics, sedatives, tranquilizers, or caffeine, may be used cautiously in reduced dosage. In emergency surgery $\frac{1}{4}$ to $\frac{1}{2}$ the usual dose of narcotics, analgesics, and other premedications should be used avoiding parenteral administration where possible. Carefully adjust dose of anesthetics to response of patient. Withdraw pargyline two weeks before elective surgery.

Warn patients about the possibility of postural hypotension. Those with angina or coronary artery disease should not increase physical activity with an improvement in well being. Pargyline may lower blood sugar.

Avoid use of enteric-coated potassium tablets, as these may induce serious or fatal small-bowel lesions consisting of stenosis with or without ulceration. These small-bowel lesions have caused obstruction, hemorrhage and perforation frequently requiring surgery. Medication should be discontinued immediately if abdominal pain, distension, nausea, vomiting or GI bleeding occurs. These products contain no added potassium salts and if added potassium intake is desired, dietary supplementation is recommended. Coated potassium tablets should be reserved for cautious use when adequate dietary supplementation is impractical. In patients with a history of allergy or asthma the possibility of sensitivity reactions should be considered.

Precautions: Measure blood pressure while patient is standing to determine antihypertensive effect. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Use with caution in patients with liver disease. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. With prolonged therapy, examine patients for change in color perception, visual fields and fundi. Also reported have been: blood dyscrasias including thrombocytopenia with purpura, agranulocytosis and aplastic anemia; elevations of BUN, serum uric acid, or blood sugar. Symptomatic gout may be induced. In surgical patients thiazides may reduce response to vasopressors and increase response to tubocurarine.

Adverse Reactions: Pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extrapyramidal symptoms have been reported in a few patients with reduced cardiac reserve.

During intensive or prolonged therapy, guard against hypochloremic alkalosis and hypokalemia (especially the latter if patient is on digitalis). Observe all patients for signs of hyponatremia ("low salt" syndrome).

Reported thiazide reactions also include anorexia, nausea, vomiting, diarrhea, headache, dizziness, paresthesia, weakness, skin rash, photosensitivity, jaundice, and pancreatitis. Nocturia has been observed with the combination.

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Untoward Reactions Associated with Antimicrobial Therapy

Part III. Metabolic and Electrolytic, Skeletal, Neuromuscular, and Dermal Reactions with
Comment and Conclusions*

Metabolic and Electrolytic

Antianabolic Effect

The tetracyclines can produce an antianabolic effect that is manifested by negative nitrogen balance, increased azotemia, hyperphosphatemia, and urinary loss of sodium, but the effect is rarely significant in patients with normal renal function.

Sodium Potassium

As briefly mentioned in Part I, some antibiotics should be used with caution in patients with cardiac or renal diseases because of the increased intake of sodium or potassium intrinsic in therapy with these drugs. For example, cephalothin has a sodium content of 55 mg/Gm. whereas each 4 Gm. of methicillin supplies 230 mg. of sodium, and each 15,000,000 units of potassium penicillin G contains 975 mg. of potassium.

Hypocholesterolemic Effect

Neomycin-induced malabsorption is a possible explanation of the hypocholesterolemic effect that follows oral administration of the drug. In a study by members of our group, patients were given neomycin for one week in a daily dose of 4 Gm. and the average decrease in the value for plasma cholesterol was 15%.¹

Glycosuria

Administration of bacitracin may result in glycosuria. Use of nalidixic acid may result in false-positive reactions for urinary glucose, and possibly true glycosuria. Cephalothin also has

caused false-positive reactions for glycosuria. The sulfonamides may have a hypoglycemic effect.

Nalidixic acid may have an antipyretic action similar to that of aspirin.

Among the multiple untoward effects of therapy with amphotericin B is hypokalemia, and determination of the concentration of serum potassium should be made periodically.

The sulfonamides may precipitate an exacerbation of porphyria hepatica in susceptible persons.

Skeletal

Despite the terminology, the syndrome of serum sickness is now caused more frequently by drugs than by serum products. Myalgia and arthralgia are frequent, but true synovitis is rare. The syndrome is usually noted within several days of receipt of the antimicrobial drug, and a penicillin appears to be most commonly responsible. In addition to the skeletal manifestations, a rash, lymphadenopathy, varied degrees of edema, fever, and other findings may occur. The reaction may subside in 48 hours, or it may persist for two weeks or more.

The tetracyclines are retained in bone, apparently because of the chelating properties of these agents and formation of a stable, insoluble tetracycline-calcium-orthophosphate complex. Ultra-violet fluorescent microscopy has revealed deposits of a tetracycline that are bright yellow in newly deposited bone, calcified cartilage, and extra-skeletal calcification. If a tetracycline is administered at a specific time before bone sampling, the amount of cortical bone formed between labeling and sampling can be measured.

*See Parts I and II, Minnesota Med. 50:1393 and 50:1571, 1967.

In rats, administration of a tetracycline during the tenth to the fifteenth day of gestation results in a considerable reduction in expected fetal size at term. As aforementioned, the question has been raised whether deposition of the drugs in bone might inhibit linear bone growth in infants, especially in those born prematurely. Fluorometry has revealed transplacental deposits of the tetracyclines throughout the human fetal skeleton. In such cases there is reversible depression of skeletal growth on short-term administration of the tetracycline.

Bulging fontanelles have occurred after administration of a tetracycline in infants, but this has disappeared on cessation of treatment.

Neuromuscular

In considering the possible neurotoxic reactions, one is impressed with the number of antimicrobial drugs that may involve the eighth cranial nerve in an untoward manner.

Vestibular Effect

Vestibular involvement may be characterized initially by some vertigo, but this is frequently difficult to verify because the patient is in bed most of the time. Also, in the initial stage, the dysequilibrium may be difficult to substantiate by physical examination, the nystagmus may be inconstant, and only vestibular-turning tests may be capable of detecting early signs of otic damage. The vestibular damage may be confirmed clinically during the subsequent two or three months, but later on the dysequilibrium usually decreases to a considerable degree, mainly because of compensatory visual mechanisms. However, the degree of compensation may not be optimal in patients of advanced age.

Cochlear Involvement

Cochlear involvement is more serious, because compensated dysequilibrium is preferable to deafness, and almost always the hearing loss is irreversible even if the treatment is stopped. Characterized at first by a decrease in hearing high frequencies, detectable only by the audiogram, the deafness proceeds progressively to conversation frequencies and hypoacusia, if treatment is continued. The obvious disproportion of the residual functional deficit between cochlear and vestibular damage accounts for the current recommendation

that one use streptomycin, which is more likely to induce vestibular toxicity, in preference to dihydrostreptomycin, which is more likely to damage the cochlear portion of the eighth nerve. Other antimicrobial drugs capable of causing cochlear damage are kanamycin, neomycin, and vancomycin. Whether ristocetin or colistin is ototoxic is uncertain. One should avoid concurrent and, perhaps, sequential use of these ototoxic drugs. The likelihood of ototoxicity is greater in infants, the aged, dehydrated patients, and those with impaired renal function. Individual susceptibility to the causative drugs may also have a role in the genesis of damage to the eighth nerve; and although the daily dose and duration of the treatment are important factors, it is almost impossible to establish absolute security against ototoxicity in all cases. Although the ototoxicity of these drugs when given intramuscularly or intravenously is well recognized, it is less well appreciated that otic damage after use of some of them has occurred from their intrapleural instillation, topical application to cutaneous burns, aerosolization, and oral administration. To avoid ototoxicity after oral administration of kanamycin or neomycin, the total daily dosage should not exceed 4 Gm.^{2,3}

Detection of early vestibular and cochlear complications can best be achieved if audiograms and vestibular-turning tests are done before, during, and at the conclusion of treatment. Also, monitoring of the serum levels of these drugs, especially in predisposed subjects, is advisable. The blood concentration of streptomycin should not exceed 25 µg/ml. and the daily dose should be adjusted accordingly. With normal renal function and in keeping with the total body weight of the recipient, ototoxic effects are generally unlikely if no more than 2 Gm. of streptomycin are given daily for no longer than 14 days, or 1 Gm. is administered daily for as long as four weeks. In order to minimize ototoxicity due to neomycin or kanamycin, blood levels should not exceed 15 µg/ml.; for an adult of average weight the daily parenteral dose is 1 Gm., and one should be hesitant to continue treatment beyond 14 days.

Optic Neuritis

Optic neuritis, with consequent impairment of vision, is observed occasionally on use of isoniazid, chloromycetin, and streptomycin;⁴ the mechanism of this complication may be related to drug-

induced pyridoxine deficiency. Use of a tetracycline may be followed by acute transitory myopia.⁵ Administration of amphotericin B has caused diplopia, and polymyxin B, colistin, and nalidixic acid have induced visual disturbances.

Cortical Irritation

Penicillin G, when given in large amounts, may cause cortical irritation, including convulsions, especially in patients with decreased renal function. Chronic brain damage may result. Since anaphylactic reactions to penicillin G may also be characterized by convulsions and result in chronic brain damage, one should perhaps be more aware of the potential neurotoxicity of the drug. Convulsions also may follow use of cycloserine (Seromycin) and amphotericin B.

Other untoward effects of cycloserine, involving the nervous system, include headache, tremor, dysarthria, paresis, and dyskinesia and generally appear within the first week or two of treatment. There are some data indicating that untoward effects of this drug are prevented or controlled by concomitant administration of pyridoxine, either alone or in combination with anticonvulsants, tranquilizers, and sedatives. The antibiotic should be used with caution in patients who have impaired renal function and is contraindicated in patients with a history of epilepsy. One should be hesitant to prescribe nalidixic acid for patients with a history of epilepsy, since stimulation of the central nervous system has occurred after the drug has been used.

Polymyxin B and colistin have caused vertigo, cerebellar ataxia, and transitory disturbances in speech, among other untoward reactions involving the central nervous system.

Intrathecal injection of antimicrobial drugs, especially when they are administered in amounts exceeding the recommended dose, may result in arachnoiditis; causative drugs have included penicillin G, streptomycin, and polymyxin B.

Psychic Nature

Untoward reactions of a psychic nature may be associated with use of different antimicrobial drugs, but usually the reactions are not specific; headache, insomnia, weakness, drowsiness, and the like may occur. However, some of these drugs can cause acute psychoses with agitation, confusion, delirium, and hallucinations among other manifestations; penicillin G, the sulfapyrimidines,

and cycloserine are potentially causative; but generally, the reaction disappears when use of the offending drug is discontinued.

Psychomotor incoordination may follow administration of certain antimicrobial drugs, such as polymyxin B, colistin, the sulfapyrimidines, and griseofulvin. In some patients the reaction is sufficiently severe to warrant the advice that they not drive vehicles or use hazardous machinery.

Peripheral Neuropathy

Peripheral neuropathy may occur during treatment with streptomycin, dihydrostreptomycin, neomycin, kanamycin, chloramphenicol, polymyxin B, colistin, nitrofurantoin, the sulfonamides, amphotericin B, and griseofulvin. Some of these drugs may induce this reaction by depletion of pyridoxine. All four extremities may be involved, and clinically one may see motor changes associated with sensory abnormalities. Absence of reflexes, gradual onset of paralysis, and serious complications such as pseudotabetic syndromes are seen mainly when treatment is not discontinued.

Streptomycin, dihydrostreptomycin, neomycin, kanamycin, polymyxin B, and colistin are commonly responsible for paresthesias, usually circumoral and of the acral parts. As an isolated finding, paresthesias are not an indication for discontinuing treatment with these drugs. Paresthesias occurring during treatment with other drugs, such as nitrofurantoin or griseofulvin, probably warrant discontinuation of therapy, for fear of inducing peripheral neuropathy.

Curariform Action

As noted previously, streptomycin, dihydrostreptomycin, neomycin, kanamycin, polymyxin B, and colistin are capable of a potential curariform action. This may result in neuromuscular block and consequent respiratory or cardiac arrest. Such an effect is most likely to occur on intraperitoneal or intrapleural administration of these antibiotics and would be most unusual when the drugs are given intramuscularly. Nevertheless, the possibility should be considered in infants, in the aged, in patients with renal disease or hypoxic states, and in those receiving certain drugs such as muscle relaxants, sedatives, narcotics, and anesthetic agents. Of course, use of these antibiotics is contraindicated in patients who may have my-

asthenia gravis. Neostigmine, 0.25 mg. given intravenously, with the dose increased as necessary, may control the neuromuscular block. Edrophonium given intravenously in amounts of 10 mg. has also been recommended. In cases of neuromuscular block due to polymyxin B or colistin, intravenous use of calcium may be more effective than neostigmine or edrophonium.

Also, as aforementioned, increased intracranial pressure with bulging fontanelles has been observed after administration of a tetracycline to infants, but the pressure has disappeared on cessation of treatment.

The Gray Syndrome

The "gray syndrome," after administration of chloramphenicol to infants has also been described previously. Among the manifestations of this complication, lethargy, flaccidity, and respiratory distress may occur.

The most common cause of *Pseudomonas* meningitis is said to be a diagnostic spinal tap. As noted earlier, these "water bacilli" are frequently present in various fluids and on medical instruments exposed to fluids. If instruments used in aspiration of the spinal fluid are exposed to solutions contaminated with *Pseudomonas* organisms, iatrogenic infection may occur. Infection with these bacilli is abetted if the patient is receiving an agent, such as a penicillin, erythromycin, or lincomycin, to which these organisms are resistant.

After intramuscular injection of certain antimicrobial agents, pain, induration, and inflammation may occur at the site. Sterile abscesses rarely eventuate. Of the penicillins, benzathine, penicillin G, ampicillin, and nafcillin appear to be most likely to produce pain on intramuscular injection. Intramuscular administration of tetracycline is more likely to produce pain than is oxytetracycline or rolitetracycline. Other antimicrobial drugs that are commonly painful on intramuscular injection are erythromycin, bacitracin, and polymyxin B. In some patients, especially when the dose of 0.5 Gm. is exceeded, pain on intramuscular injection of cephalothin may require addition of a local anesthetic agent to the solution.

Arthus Phenomenon

The Arthus phenomenon may progress to an extensive hemorrhagic necrosis and ulceration, extending into the muscle. However, since the reaction is rare, at least in its more pronounced

manifestations, one should be reticent in concluding that a given lesion exemplifies the phenomenon. Lesions simulating the reaction and occurring more commonly may be due to intrinsically irritating properties of the injected drug or to secondary infection at the injection site.

As aforementioned, the sulfonamides are capable of precipitating exacerbations of porphyria in susceptible persons, and involvement of the nervous system in such patients is not infrequent. Also, the sulfonamides and numerous other drugs may be responsible for aggravation of disseminated lupus erythematosus, and various neural deficits may be among the clinical findings.

So-called drug fever may occur on administration of any antimicrobial drug. It has been postulated that this reaction might be of central origin, but there appears to be no precise evidence of a direct effect on the thermal centers. The reaction usually is believed to be a hypersensitivity one; conceivably, products released by injured cells of the "shock organs" involved might indirectly affect the thermal centers.

Dermal

Dermal reactions, including angioneurotic edema and contact dermatitis, may occur after the use of any antimicrobial drug, but among those commonly used, streptomycin, the tetracyclines, and erythromycin are least likely to be causative; conversely, the penicillins, novobiocin, and the sulfonamides are most likely to be causative. Within several days of receipt of an antimicrobial agent there may occur pruritus followed by a rash which may be erythematous, morbilliform, petechial, or purpuric, but is most commonly urticarial. Purpuric lesions may be more frequent after administration of the penicillins, novobiocin, and the sulfonamides. Most dermal reactions subside within a few days after discontinuation of therapy with the offending antimicrobial drug, but rarely the process eventuates in a more serious condition, such as exfoliative dermatitis.

Novobiocin is clinically about as effective as erythromycin against susceptible organisms, but the chief objection to its use is the occurrence of allergic dermatitis in 5 to 10% of patients receiving the drug.

Arthus Phenomenon

The Arthus phenomenon may progress from a

red erythematous area at the site of injection of an antimicrobial drug to an extensive hemorrhagic necrosis and eventual ulceration of subcutaneous tissue and even muscle.

The Stevens-Johnson syndrome (erythema multiforme exudativum) has been noted after the use of certain antimicrobial drugs that include the sulfonamides and novobiocin.

Administration of nitrofurantoin is rarely followed by transient alopecia.

Fluorescence and Photosensitivity

In patients having received prolonged therapy with the tetracyclines, fluorescence of the proximal part of the nails may be demonstrable. Sometimes significant discoloration and onycholysis can be seen with the naked eye.⁶

Photosensitivity, manifested by marked erythema with or without edema, while more frequently associated with the use of demethylchlor-tetracycline, was reported early in the experience with chlortetracycline and more recently on administration of tetracycline and oxytetracycline. Griseofulvin, nalidixic acid, and certain sulfonamides may also be photosensitizing.

As mentioned earlier, *Pseudomonas* organisms exemplify the so-called water bacilli which may contaminate various fluids. *Pseudomonas* bacteremia may follow local application of contaminated medications applied to various dermal diseases and injuries, such as eczematoid dermatitis and extensive burns.

Disseminated lupus erythematosus may be precipitated by several antimicrobial drugs, but probably a penicillin or a sulfonamide has been most commonly responsible. Porphyria, especially in the form of cutanea tarda, may also be precipitated by use of a sulfonamide.

Comment

In the light of our present knowledge, the mechanism involved in the genesis of many untoward reactions to antimicrobial drugs is believed to depend on antigen-antibody combinations, which may attack certain cells selectively for reasons that are not entirely clear. Unlike foreign proteins, antimicrobial drugs are not complete antigens and probably combine in the host's body with protein in a hapten-like manner in order to become antigenically effective. Development of hypersensitivity reflects contact with the allergen

and the individual's capacity for sensitization, which is constitutionally or genetically determined.

Allergic Reactions

Among antimicrobial drugs, the penicillins are the leading cause of allergic reactions. Cross-allergenicity among the semisynthetic and natural penicillins apparently is reflective of the fact that they share the 6-APA nucleus. It is theorized that a catabolic product, or products, of the penicillins (penicilloyl compounds as an example) may unite with body protein and cause most of the allergic reactions. The anticipation of an allergic reaction, a history of adverse reactions to a penicillin in the past, or the report that the patient previously exhibited other manifestations of allergy, particularly asthma, remain important despite the increasing validity of various tests. There are three drugs of adjunctive use that can cause allergic reactions and hence confusion with those produced by penicillin G; these are procaine, probenecid (Benemid), and penicillinase.

Cross-Resistance

Partial or one-way bacterial cross-resistance among streptomycin, neomycin, kanamycin, and paromomycin is usual; streptomycin-resistant strains may be susceptible to the other drugs, but organisms insensitive to neomycin, kanamycin, or paromomycin usually resist streptomycin as well. Generally there is complete cross-resistance among organisms able to resist neomycin, kanamycin, and paromomycin. It is thus apparent that indiscriminate use of any of these drugs is to be avoided in order to minimize the development of bacterial resistance to them. It is to be noted that bacterial resistance to neomycin has increased in recent years, apparently because the drug has been incorporated in procedures used to prepare the colon preoperatively, and because neomycin is a constituent of various preparations for local use, such as creams and ointments.

The incidence of nausea and vomiting after oral use of the tetracyclines is reduced if the agent is given with cold pasteurized milk, which may be undesirable, however, in patients receiving a low-residue or low-sodium maintenance diet. Milk may depress the concentration of drug in the blood and cannot be tolerated by some individuals. In such circumstances, calcium carbonate in amounts of 5 grains with each capsule of the antibiotic is substituted. Although calcium carbonate,

like calcium-containing foods and other antacids, may hinder the absorption of the tetracycline, blood levels usually are higher than when one resorts to the alternative of reducing the dose of the antibiotic.

Because the tetracyclines are retained in mineralized tissues, including neoplastic bone, these drugs may have potential use in determining the level of amputation in osseous tumors. The affinity of the tetracyclines for tumor cells is also being investigated, and tetracycline-fluorescence of malignant tissue may complement conventional procedures in the study of tumors of the urinary bladder, and in search of neoplastic cells in sputum and in gastric, duodenal, pleural, and ascitic fluids. Also, a tetracycline tends to accumulate in damaged but still viable tissue; consequently, the radioactivity of a tagged tetracycline may help indicate ischemic areas, such as those in the myocardium and kidney, and might help define the extent of burns.

Because of the possibility that L-phenylalanine may ameliorate chloramphenicol-induced hematotoxicity, there has evolved the hypothesis that, in some cases at least, the untoward effects of chloramphenicol on the bone marrow may be due to diminished absorption of phenylalanine from the intestinal tract rather than to a direct cellular effect of the drug. However, as aforementioned, some workers disagree with the conclusion that L-phenylalanine has a salutary effect in cases of chloramphenicol-induced hematotoxicity.

Erythromycin base is almost unique among antimicrobial drugs because of the paucity of untoward reactions associated with its use.⁷ Mild gastrointestinal irritation may follow oral use of the agent, but there is little evidence of serious allergic reactions to erythromycin base. Among the kindred drugs, hepatic dysfunction, which may follow use of erythromycin estolate and triacetyloleandomycin, limits the wider use of these agents. The relatively high incidence of allergic dermatitis militates against more common use of novobiocin. There has been insufficient study of lincomycin to allow precise assessment of its toxicity, but d'arrhea has required discontinuation of its use in 2 to 3% of patients, and hepatotoxicity, neutropenia, and superinfection are possible complications of its use.

If the production of less pain on intramuscular injection is taken as a paramount advantage of colistin over polymyxin B, one should recall that

employing a 1 to 2% solution of procaine (Novocain), lidocaine (Xylocaine), or a similar preparation in making dilutions of polymyxin B will provide the same effect. Except for the consideration of pain at the injection site, the untoward reactions after use of these two drugs are virtually identical in type and degree, although it has been suggested that colistin may have additional forms of toxicity.⁸

Among the less commonly employed antimicrobial drugs are the nephrotoxic bacitracin, the ototoxic vancomycin, the hematotoxic ristocetin, and the neurotoxic cycloserine. Today these drugs are less commonly used for their systemic effect, because effective drugs that are less toxic have become available. However, in patients allergic to the penicillins, who have serious staphylococcal infections, such as endocarditis, some workers prefer vancomycin to cephalothin.

A difficulty with the use of cephalothin stems from an apparent dichotomy between in-vitro bacterial susceptibility and in-vivo achievability, especially in infections due to certain strains of staphylococci, *Neisseria*, *Salmonella*, *Shigella*, and *Haemophilus influenzae*.

It appears to remain the consensus among physicians with a special interest in infectious diseases that a significant degree of cross-allergenicity between cephalothin and the penicillins is unlikely, but the possibility is not entirely excluded. Some patients allergic to the penicillins have had untoward reactions to cephalothin, but a goodly number have not; in this regard, it should be recalled that patients allergic to the penicillins have taken the drugs at a later date without untoward incident.

Cephalothin, while evidently resistant to staphylococcal penicillinase, may be degraded by a similar enzyme, cephalosporinase, which is also of bacterial origin. Cephalosporinase, like penicillinase, appears to be a beta-lactamase which acts on the beta-lactam ring of cephalothin. It is not agreed at present whether organisms produce different beta-lactamases, some with primarily cephalosporinase activity, or produce only one enzyme which has varying cephalosporinase-penicillinase ratios. In any event, if such enzymes cause future clinical problems, such as contributing to bacterial resistance, there is the possibility of synthesizing cephalosporinase-resistant cephalosporins.

The sulfonamides currently available are undoubtedly less toxic than those employed previously, but it is well to remember that any of them can conceivably be responsible for such untoward reactions as nephrotoxicity, blood dyscrasias, the Stevens-Johnson syndrome, and periarteritis nodosa. Anaphylaxis, hepatitis, pancreatitis, cyanosis, purpura, conjunctivitis, and "serum sickness" are uncommon with the compounds in current use. Cross-hypersensitivity to various sulfonamides, as well as to chemically related drugs (for example, tolbutamide), is common. The decreased detoxification of the sulfonamides in patients with hepatic dysfunction should be borne in mind.

Use of methenamine mandelate (Mandelamine) may cause gastrointestinal irritations and skin rashes; the drug is contraindicated in renal insufficiency. It is recommended that methenamine mandelate not be given conjointly with the sulfonamides, because sulfamethizole and sulfathiazole may form an insoluble precipitate with formaldehyde in the urine.

Among the nitrofurans, nitrofurantoin and furazolidone (Furoxone) may produce a disulfiram-type reaction; consequently patients receiving these drugs should be advised to refrain from ingestion of alcoholic drinks. So-called nitrofuran neuropathy⁹ is usually reversible but not invariably so.

Nalidixic acid is capable of potential untoward reactions involving several systems of the body. Among these reactions are visual disturbances, stimulation of the central nervous system, possible hepatotoxicity, increased azotemia, and photosensitization. Because of these reactions and because the drug's antibacterial spectrum is virtually limited to *Escherichia coli*, the long-term application of the drug is somewhat questionable. Strains of *E. coli*, resistant to nalidixic acid, have emerged during therapy, and bacterial resistance to nalidixic acid appears to increase in a given environment in direct proportion to the amount of the drug employed therein.

Amphotericin B must be numbered among the drugs with the highest potential for untoward reactions, and these run the entire gamut of the bodily systems.¹⁰ The drug continues to be employed because it is effective, and there is no alternate drug in most diseases of mycotic or fungal origin.

Nystatin, which is not absorbed from the gastrointestinal tract but is sometimes given orally in

an attempt to combat candidal enterocolitis, may cause nausea, vomiting, and diarrhea but rarely causes untoward reactions of a systemic nature.

Griseofulvin, which is absorbed from the gastrointestinal tract, represents a distinct step forward in the management of susceptible fungal infections. However, it may cause untoward reactions involving several systems of the body; these effects include peripheral neuropathy, photosensitization, and gynecomastia. Because griseofulvin is derived from species of *Penicillium*, the possibility of a cross-sensitivity reaction exists.

Because of the ever-increasing ability of man to synthesize (or semisynthesize) effective antimicrobial drugs, an apparent advantage provided by a chemical change in a drug may be accompanied by disadvantages that are not characteristic of the parent compound and which therefore may not be immediately evident. The unexpected hepatotoxicity due to the propionyl ester of erythromycin and that due to triacetyloleandomycin are examples of undesirable effects, not characteristic of the parent drugs, which may accompany a chemical change in an antimicrobial drug that initially appeared to represent a more desirable product. Other examples of this phenomenon include the increased photosensitizing capacity of demethylchlortetracycline and the greater incidence of nephrotoxic and hematotoxic reactions associated with the use of methicillin, when compared with use of the parent drugs.

Conclusions

All antimicrobial drugs are capable of provoking untoward reactions, and almost any organ in the body may be involved. However, the ability of individual antimicrobial drugs to result in untoward reactions is variable and ranges from the minimal capacity of erythromycin to that of amphotericin B, which is capable of causing multiple ill effects and of affecting virtually every system of the body. Fortunately, the antimicrobial drugs that are most commonly employed are intermediate in their capacity to provoke untoward reactions. As a consequence of the increasing number of new antimicrobial drugs or chemical modifications of older ones, continuous reevaluation of the totality of these drugs is essential, because the benefits, as well as the untoward reactions, may not become evident for months or years after their clinical introduction. Unfortu-

nately, the tendency of patients to exhibit an untoward reaction to an antimicrobial drug cannot be precisely predicted prior to its administration. Previous exposure to an antimicrobial drug is often responsible for an untoward reaction to its use, but some patients experience such a reaction on their first exposure to a therapeutic dose of the drug. Many untoward reactions could be avoided, however, if antimicrobial drugs were used only when indicated and if adequate consideration were given to known preventive aspects. Among the

measures that may minimize the untoward reactions to these drugs are: (1) questioning of the patient to elicit a history of previous untoward reactions to a drug or associated allergies, (2) familiarity with the proper dose of a drug for the patient at hand, (3) awareness of the untoward reactions associated with use of a given drug and their early detection, and (4) employment of a drug only for conditions in which it has known therapeutic value.

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References

1. Nunn, S. L., Schirger, A., Martin, W. J., Juergens, J. L., Tauxe, W. N., and Osmundson, P. J.: Effect of Neomycin on Human Biosynthesis of Cholesterol (P). (Abstr.) *Circulation* 28:780, 1963.
2. Kunin, C. M., Chalmers, T. C., Leevy, C. M., Sebastyen, S. C., Lieber, C. S., and Finland, M.: Absorption of Orally Administered Neomycin and Kanamycin With Special Reference to Patients With Severe Hepatic and Renal Disease. *New Engl J. Med* 262:380, 1960.
3. Last, P. M., and Sherlock, S.: Systemic Absorption of Orally Administered Neomycin in Liver Disease. *New Engl J Med* 262:385, 1960.
4. Walker, G. F.: Blindness During Streptomycin and Chloramphenicol Therapy. *Brit J Ophthal* 45:555, 1961.
5. Edwards, T. S.: Transient Myopia Due to Tetracycline. *JAMA* 186:69, 1963.
6. Segal, B. M.: Photosensitivity, Nail Discoloration, and Onycholysis: Side Effects of Tetracycline Therapy. *Arch Intern Med (Chicago)* 112:165, 1963.
7. Herrell, W. E., Nichols, D. R., and Martin, W. J.: Erythromycin for Infections Due to *Micrococcus pyogenes*. *JAMA* 152:1601, 1953.
8. Katz, R.: Renal and Possibly Hepatic Toxicity From Coly-Mycin: Report of a Case. *Med Ann DC* 32:408, 1963.
9. Martin, W. J., Corbin, K. B., and Utz, D. G.: Paresthesias During Treatment With Nitrofurantoin: Report of Case. *Mayo Clin Proc* 37:288, 1962.
10. Martin, W. J., Nichols, D. R., Svien, H. J., and Ulrich, J. A.: Cryptococcosis: Further Observations and Experiences With Amphotericin B. *Arch Intern Med (Chicago)* 104:4, 1959.

Carotid-Pressure Anesthesia

Greek physicians knew the ancient art of producing unconsciousness by pressing on the carotid arteries in the neck. As a matter of fact, the very name carotid comes from the Greek word *karoun* which means heavy sleep.

Even Aristotle wrote in his *History Of Animals*: "If these veins are pressed externally, men, though not actually choked, become insensible and shut their eyes and fall flat on the ground."

Pressure anesthesia, known from prehistoric times, was revived again when Ambroise Pare used this method as early as 1543.

About a year later, it was used by Realdo Colombo in Pisa. As described by the Spanish physician, Valverde, who was present, this was a strange performance. "The carotids," he wrote, "that is, the sleep-producing arteries, are so named because when they are pressed upon or closed up in any way we soon go to sleep. This experiment I saw performed by Realdo Colombo in 1544 in Pisa, on a young man in the presence of a number of gentlemen, with no less fear on their part than amusement on ours, for we gave them to understand that it was done by sorcery."*

*Bernard Seeman: *Man Against Pain*.

His handshake ought not to be used except as a tourniquet.

Margaret Halsey

Night Leg Cramps . . . Unwelcome Bedfellow In Diabetes,¹ Arthritis,² and Peripheral Vascular Disorders²

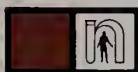


now . . . specific therapy for night leg cramps

Walker

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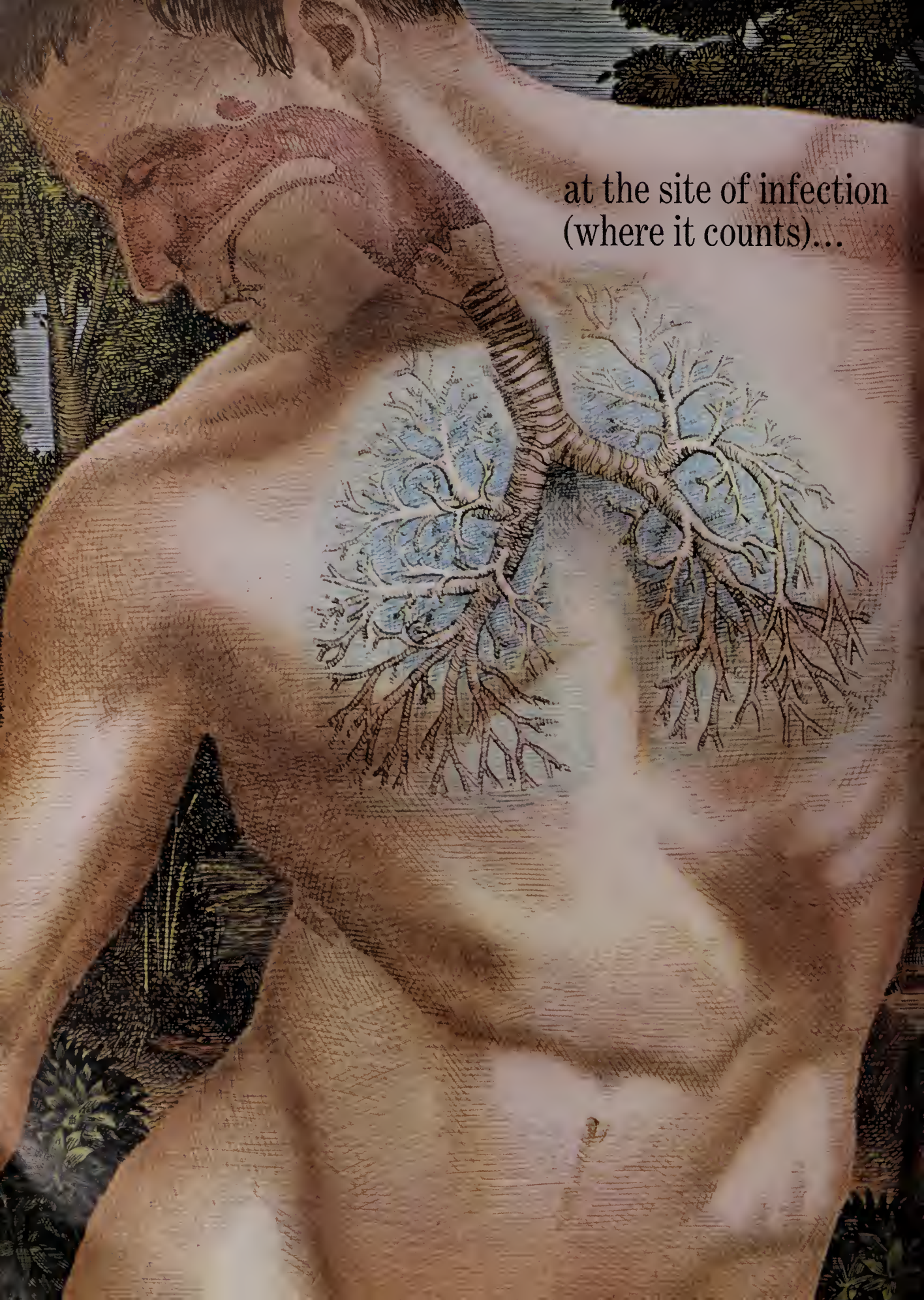
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Penicillin is the drug of choice for syphilis and gonorrhea, but Ilosone in multiple 500-mg. doses has been useful in patients with a history of penicillin allergy. Also, other infections due to susceptible bacteria in patients hypersensitive to penicillin or other antibiotics may be considered for treatment with Ilosone.

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In syphilis, a total of 20 to 30 Gm. is administered in divided doses for ten to fifteen days. Close follow-up is necessary since erythromycin drugs have not had adequate evaluation in all stages of syphilis. Examination of spinal fluid is recommended during follow-up.

In gonorrhea, the dosage is 500 mg. four times a day for four days. Patients with a suspected lesion of syphilis should have a dark-field examination before receiving antibiotics and monthly serologic tests for three months. For detailed information, consult the package literature.

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[080967]

References: 1. Griffith, R. S., and Black, H. R.: *Am. J. M. Sc.*, 247:69, 1964. 2. Griffith, R. S., and Black, H. R.: *Antibiotics & Chemother.*, 12:398, 1962. 3. Hirsch, H. A., Pryles, C. V., and Finland, M.: *Am. J. M. Sc.*, 239:198, 1960.

Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana 46206.



701464



Grand Rounds

Hashimoto's Thyroiditis*

ROBERT NOTSKE, M.D.

Medical Resident

IN 1912 HASHIMOTO described four patients with a chronic disorder of the thyroid which he termed struma lymphomatosa. The thyroid glands of these patients were characterized by diffuse lymphocytic infiltration, fibrosis, parenchymal atrophy, and an eosinophilic change in some of the acinar cells.¹ Frequent clinical and pathological studies of this disease have appeared since Hashimoto's original description. The disease has variously been called "Hashimoto's disease," "chronic thyroiditis," "lymphocytic thyroiditis," "lymphadenoid goiter," and recently "auto-immune thyroiditis."

Incidence

Typically, the disease occurs as a painless diffuse enlargement of the thyroid gland in a young or middle-aged woman, often associated with hypothyroidism. Whether the pathologic lesion is the result of one causative agent or many is still unknown. The disease was thought to be uncommon for many years, and the diagnosis was usually made after thyroidectomy or at autopsy. The increasing use of thyroid needle biopsy has led to its more frequent recognition, and some investigators believe it may be increasing in frequency.² The true incidence in the general population is not known, but it is certain that it exists with a much higher frequency than is diagnosed clinically.

The disease is fifteen to twenty times as common in females as in males and occurs especially during the decades from 30 to 60 but may be seen in any age group, including children. DeGroot et al. have reported a number of relatives of patients with Hashimoto's thyroiditis, with moderate enlargement of the thyroid gland and positive antibody studies, but who are entirely

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, January 17, 1967.

asymptomatic. This suggests the possibility of a much higher incidence than is reported.

Pathology

Grossly the tissue involved by Hashimoto's disease is a pinkish-tan to frankly yellowish, and tends to have a rubbery firmness. The goiter is generally quite symmetrical, often with a conspicuous pyramidal lobe. The capsular surface is gently lobulated and non-adherent to perithyroid structures.

Microscopically, one typically sees a diffuse process consisting of a combination of parenchymal atrophy and lymphoid cellular infiltration. The thyroid cells tend to be slightly larger and assume an oxyphilic staining character; they are then called Askanazy cells. The follicular spaces are shrunken, and the colloid is absent or sparse. Within the follicles may be seen clusters of macrophage-like cells. The lymphoid infiltration in the interstitial tissue is accompanied by follicles and germinal centers. Plasma cells are occasionally prominent. Fibrosis may be completely absent or present in degrees ranging from slight to moderate, but rarely severe, as observed in subacute thyroiditis or Riedel's thyroiditis. Foreign body giant cells and granulomas are not features of Hashimoto's disease, in contrast to subacute thyroiditis.

The quantity of parenchymal tissue left in the thyroid is variable. In some instances it is increased, perhaps in a hyperplastic compensatory response to inefficient iodide metabolism.

In addition to the typical disease in which the pathologic process involves the entire lobe or gland, focal thyroiditis which is microscopically similar may be found in the thyroid with diffuse hyperplasia of Graves' disease, in association with thyroid tumors, or in multinodular thyroid glands.¹

Physical Findings

A diffuse, firm goiter with pyramidal lobe enlargement and without signs of thyrotoxicosis should suggest the diagnosis. The association of goiter with hypothyroidism is almost diagnostic of this condition, but it is seen in certain other thyroid conditions. Pain and tenderness are unusual but may be present. A rapid onset is unusual, but the goiter may grow from normal to several times normal size in the period of a few weeks. Most commonly the gland is two to four times normal size. Satellite lymph nodes may be present, especially the "Delphian" node above the isthmus.¹

Laboratory Findings

Laboratory studies may at times be as confusing as helpful. The basal metabolic rate is normal or depressed. The protein-bound iodine concentration ranges from low to high but is most typically in the normal or low range. Characteristically, the butanol extractable iodine is significantly lower than the protein-bound iodine.^{4,5} Radioactive iodine uptake is variable⁶ and ranges from below normal to elevated values, depending on such factors as thyroid-stimulating hormone production by the pituitary, the efficiency of utilization of iodide by the thyroid, and the nature of the component being released into the peripheral circulation.⁷ Plasma albumin is decreased and gamma globulin is elevated. Cephalin flocculation or thymol turbidity tests are abnormal.⁸ The erythrocyte sedimentation rate is usually elevated.

Antibodies to thyroglobulin are present in the serum.^{9,10,11,12} Titers of 80,000 or more are virtually diagnostic of Hashimoto's thyroiditis.¹³ Tanned red cell antibodies are detected in 80 per cent of patients, and with the addition of the complement fixation test, 97 per cent of patients are positive.¹⁴ In young patients, typical Hashimoto's thyroiditis may be present with low titers of antibodies.¹⁵ Thus low titers in this age group do not rule out the disease.

At the Mayo Clinic¹⁶ and Massachusetts General Hospital¹ the most useful approach has proven to be the needle biopsy. The involved thyroid usually has a firmness that makes it relatively easy to biopsy. The whitish plug of tissue is almost diagnostic of Hashimoto's thyroiditis upon gross inspection in a clinically suggestive case.

Pathogenesis

Hashimoto's thyroiditis usually begins as a gradual enlargement of the thyroid gland. It is often discovered by the patient, who find a fullness of the neck or who discovers a new lump while examining himself because of vague discomfort in the neck. Occasionally it is found by a physician during the course of examination for some other complaint.

In some instances thyroid enlargement may be rapid and associated with dyspnea and dysphagia related to pressure on structures in the neck. Occasionally the course is clouded by symptoms of mild thyrotoxicosis, especially during the early phases of the disease. The goiter may remain unchanged for decades¹⁷ but usually increases gradually in size. Symptoms and signs of hypothyroidism commonly develop over a period of years. Eventual thyroid atrophy and myxedema may occur. This assertion is based on the clinical observation that patients with Hashimoto's thyroiditis occasionally develop myxedema, and the knowledge that patients with myxedema due to atrophy of the thyroid have a high incidence of antithyroglobulin antibodies in their serum.¹⁸

The pathophysiology is failure of thyroid cell function resulting in thyroxine deficiency. Apparently, a less calorigenically active thyroglobulin is released, which produces a normal-to-slow increase in protein-bound iodine and is also capable of eliciting an antibody response. This globulin is believed to leak out of cells because of their increased permeability. Later the protein-bound iodine falls as the cells continue to fail. The thyroxine deficiency results in an increase in thyroid-stimulating hormone which may cause a high radioactive iodine uptake. As the ability of the thyroid to trap iodine falls, the radioactive iodine uptake also falls and does not respond to thyroid-stimulating hormone stimulation. Apparently, failure to produce thyroxine occurs before failure to trap iodide. The amount of intrathyroidal exchangeable iodide is abnormally low; therefore, a rapid turnover and high conversion ratio may occur.⁷

The glands of Hashimoto's patients do not bind iodide as efficiently as normal glands.¹⁹ Administration of 400 mg. potassium perchlorate one hour after an I^{131} tracer releases 20 to 60 per cent of the accumulated iodide. There is also evidence of the presence of an abnormal peptide-linked iodinated component.^{3,20,10,21} This is thought to be a distinct iodoprotein rather than a fragment of thyroglobulin.

Buchanan²² has thoroughly studied iodide metabolism in Hashimoto's thyroiditis. He found the I^{131} uptake and clearance rates to be variable.

Plasma inorganic iodide and uptake of stable iodide were normal. The intrathyroidal exchangeable iodine and the efficiency of utilization of trapped iodide by the thyroid both tended to be low. There was also found an increased proportion of plasma organic iodide which was butanol-insoluble.¹⁸

The concept developed from this data is that the diseased gland releases some trapped iodide back to plasma without incorporating it into organic compounds; has a diminished ability to maintain normal thyroid iodide stores; and has a high turnover rate if the exchangeable iodine pool of the gland is low. It also releases non-hormonal organic iodide into the circulation. Because of this inefficient utilization of iodide, the gland is under increased thyroid-stimulating hormone stimulation.

Differential Diagnosis

The differential diagnosis is that of nontoxic nodular goiter. The presence of gross nodularity is against thyroiditis, but not infallible. In nontoxic nodular goiter, function tests are usually normal and hypothyroidism is unusual. Antibody titers are less apt to be high.

Enlargement of thyroid during adolescence¹⁵ is usually due to hyperplasia of thyroid in response to temporarily augmented demand for hormone. Here again function tests should be normal.

Tumor must be considered. The diffuse nature of thyroiditis, the characteristic hypothyroidism, and involvement of the pyramidal lobe are usually sufficient to allow differentiation. Biopsy may prove of little value, since lymphoma or a small-cell carcinoma of the thyroid can be and has been mistaken for Hashimoto's thyroiditis. Lymphosarcoma has been reported in Hashimoto's,^{23,16} and papillary carcinoma has been reported as being associated with the disease.^{16,21} Carcinomas have also been reported in other areas apart from the area of a focal thyroiditis found on biopsy.

Occasionally, Hashimoto's thyroiditis may present as a mild thyrotoxicosis; however, T_3 suppression usually provides the necessary information to make a diagnosis.

Therapy

Many patients need no therapy at all if the disease is asymptomatic and the goiter small; but these patients should be followed for signs of hypothyroidism. Vickery and Ham'in¹⁷ found on serial biopsies that the disease usually remains static for years.

If the gland is of the size to cause pressure symptoms, thyroid hormone usually reduces the size of the goiter over several months.²⁵ In young people with less fibrosis the response has been noted in two to four weeks.

In those cases with rapid development of goiter and pain, steroids have been used both to decrease the inflammatory response and to depress the antibody titer.²⁶

If hypothyroidism is present, replacement therapy with thyroid hormone is mandatory.

Surgery appears to be indicated for pressure symptoms or cosmetic reasons in goiters not responding to medical treatment. It is also indicated in the case of a growing nodule in a young person which does not metabolize I^{31} in a normal fashion.¹ However, if findings suggestive of thyroid carcinoma are not present, medical management with thyroid hormone is the

treatment of choice.

Auto-Immunity

The frequent occurrence of elevated serum levels of gamma globulin, a delay in return to normal levels after thyroidectomy, infiltration of the thyroid substance with lymphocytes and plasma cells, and the not uncommon incidence of Hashimoto's disease with known auto-immune diseases suggest an immune basis for this disease.

Rose and Witebsky²⁷ showed that immunization of rabbits with extracts of their own thyroid tissue produced histologic changes in the thyroid glands resembling those seen in Hashimoto's disease. They also found that antibodies to thyroglobulin could be detected in the blood. Roitt et al.¹¹ observed that a precipitate forms when serum from a patient with Hashimoto's disease reacts with an extract of human thyroid gland. This indicated to them that the serum contained antibodies to a constituent of the human thyroid and that these antibodies might be responsible for the disease process.

Four auto-antigens have been identified in the sera of patients with Hashimoto's thyroiditis. Precipitating antibodies were first identified. With agar gel diffusion or Ouchterlony plate technique they can be demonstrated. Using the tanned red cell hemagglutination test of Boyden²⁸, antibody could be detected at 1/40,000, the titer required to give a positive precipitin reaction. Titers as high as one in five million have been obtained from sera of patients with chronic thyroiditis. Usually a high antithyroglobulin titer of one in 80,000 or more is presumptive evidence of Hashimoto's disease and helps to distinguish it from multinodular goiter and thyroid carcinoma.^{11,12,13} This test is still negative in 10 to 20 per cent of histologically proven cases. So a negative result does not rule out the disease. In ten per cent of women aged 40 to 60, low titers have been found.¹⁵

A second distinct immune system has been identified in patients with Hashimoto's disease. These antibodies fix complement in presence of extracts from thyrotoxic glands and are directed against the microsomal fraction of thyroid cells.²⁹ These same sera have also been shown to have a high cytotoxic activity on trypsinized thyroid cells in tissue culture.³⁰ Whether these antimicrosomal antibodies and the cytotoxic factor are identical has not yet been shown.

The fluorescent antibody technique has been applied to the study of antigen-antibody reaction in the thyroid.³¹ An antibody solution of high titer is conjugated with fluorescein isocyanate, and wherever antigen-antibody precipitates form, the fluorescein-stained complex is fixed and can be localized under a microscope. This method can be used to locate complexes, or as qualitative or quantitative tests. A fluorescein conjugate of the globulin obtained from the serum of patients with Hashimoto's disease reacts not only with normal thyroid, but also with his own gland. This reaction corresponds to the complement-fixing microsomal antibody as shown by the fact that prior absorption of the microsomal fraction inhibits the staining.

In serums of certain patients with Hashimoto's disease, fluorescent antibody technique has also demonstrated a localization of the reaction to the nuclei of the thyroid slice. This is thought to tie in with the frequency of Hashimoto's disease occurring in patients with known immune diseases.

Also using fluorescent antibody techniques an antibody has been seen in the colloid component other than thyroglobulin.

Antithyroglobulin antibodies can be demonstrated by passive cutaneous anaphylaxis technique in guinea pigs.³² Also a skin test has been developed by Buchanan et al.³³; but its use as a routine test is hampered by the risk of serum hepatitis from injection of the extract of thyroid gland.

Several theories have been advanced to explain the auto-immune reactions of Hashimoto's disease. The first involves an abnormality in immune homeostasis in the body, such as failure to properly sequester thyroid antigens from the lymphoid tissue. Evidence for this theory is obtained from the studies of Sommers and Meissner³⁴ who examined the thyroid basement membrane from 70 patients including normal controls, chronic thyroiditis, thyrotoxicosis and thyroid carcinoma. In every instance of thyroiditis there were diffuse abnormalities of the thyroid membrane not only at the location of infiltration but also in remote areas of the gland without infiltrate. In the tissue of the thyrotoxic glands, if there was a lymphocytic infiltrate there were also basement membrane abnormalities. Stuart and Allen³⁵ confirmed the basement membrane lesion in patients with a high circulating antibody level. They found good correlation between the presence of basement membrane lesion and high circulating antibody levels, and no basement membrane lesion in low antibody levels. Although it is an attractive hypothesis that a lesion of the basement membrane precedes and is responsible for the auto-immune process, it is entirely possible that the basement membrane defect is secondary to this process.

The second proposed theory of auto-immunity is a genetically determined capacity for producing auto-antibodies. Support for this theory comes from the association of known auto-immune diseases with thyroiditis. Reports have been published of association between thyroiditis and Sjögren's syndrome,^{34,36} rheumatoid arthritis,³⁷ systemic lupus erythematosus,³⁸ Addison's disease,^{39,40} lipid hepatitis,⁴¹ and portal cirrhosis of the liver in which an identical extensive lymphocytic and plasma cell infiltrate was found in both the liver and the thyroid. In all of the disorders associated with Hashimoto's disease, abnormalities of the immune mechanism have been postulated. Many of the features of these diseases could be explained on the basis of excessive sensitivity of the immune apparatus, resulting in a breakdown in the immune tolerance to the body's own antigens. Such an abnormality of the immune mechanism could possibly result from a genetic defect, as evidenced by the overlap in these diseases, both in the individual and in families.

The third theory proposes an abnormal antigen, which may be either congenital or acquired. Complement fixing and antithyroglobulin antibodies have been found not only in patients with Hashimoto's, but also in their parents

TABLE

	Ra I %	AB titer	PBI Mcg %	BMR	Ceph. Floc.	Chol Mg %	Biopsy	Proteins	ESR	Symptoms
M.M., 52	—	1:256	5.0	—	—	350	—	—	30	Pressure
N.M., 63	9.9	—	3.0	-5% -6%	—	265 357	Thyroiditis. (2 nodes)	—	—	Pressure
G.H., 47	17.6	—	2.9 2.6	+9%	Neg	210	Thyroiditis. (1 node)	4.2/3.6 Neg FANA	97/122	Lump
M.C., 53	18.9	—	3.2 2.1	+10%	Neg (T26)	280 350	Thyroiditis	—	66	Nervousness
S.S., 64	2.1	—	6.9	—	—	190	Thyroiditis	—	85	Hoarse voice. Lump
A.O., 31	22.3	—	6.4 2.3	—	—	—	Thyroiditis. (1 node)	3.3/2.9	—	Pressure
M.P., 53	21.1	—	5.0	-18%	—	—	Thyroiditis	—	23	Nodule

and siblings.^{42,43,44} In fact, the disease has been shown in both members of two sets of uniovular twins. It has also been shown that in some patients with Hashimoto's thyroiditis a circulating iodoprotein can be demonstrated similar to that seen in one group of goitrous cretins.⁴⁵ Organification of iodine is sometimes defective in Hashimoto's disease.

Possibly the initial insult to the thyroid results from congenital dysor-monogenesis, a virus infection, thyrotoxicosis, etc. The end picture in each instance would be a nonspecific end of Hashimoto's disease. Since this chain of events does not normally occur in these cases, some overactivity of the immune mechanism would seem to be an additional requisite.

Hennepin County General Hospital Experience

The Table depicts seven cases of Hashimoto's thyroiditis at Hennepin County General Hospital. There were biopsy diagnoses made at surgery on six out of seven cases. The only case not operated had an antithyroglobulin titer of 1:256. Although this is not the diagnostic value reported in the literature, it was significant for the laboratory performing the test.

References

1. Means, J. H., DeGroot, L. J., Stanbury, J. B., The Thyroid and Its Diseases, McGraw-Hill Book Co., Inc., New York, 1963.
 2. McConahey, W. M., Keating, F. R., Jr., Beahrs, O. H., and Woolner, L. B. J Clin Endocr 22:542, 1962.
 3. DeGroot, L. J., Hall, R., McDermott, W. V., Jr., and Davis, A. M. New Engl J Med 267: 267, 1942.
 4. Skillern, P. G., Crile, G., McCullagh, E. P., Hazzard, J. B., Lewis, L. A., and Brown, H. J. Clin Endocr 16:35, 1956.
 5. Beare, R. L. B Brit Med J 1:480, 1958.
 6. Murray, I. C., McGirr, E. M. Brit Med J 1:838, 1960.
 7. Doniach, D., and Hudson, R. V. Brit Med J 1:672, 1957.
 8. Luxton, R. W., and Cooke, R. T. Lancet 2:105, 1956.
 9. McConahey, W. M., Keating, F. R., Butt H. R., and Owen, C. A. J Clin Endocr 21:879, 1961.
 10. Blizzard, R. M., Hamwi, G. J., Skillman, T. G., and Wheeler, W. E. New Engl J Med 260: 112, 1959.
 11. Roitt, I. M., Doniach, D., Campbell, D. N., Hudson, R. V. Lancet 2:820, 1956.
 12. Goudie, R. B., Anderson, J. R., Gray, K. G., Clark, D. H. Murray, I. P. C, and McNicol, G. P. Lancet 2:976, 1957.
- 13-45 May be secured from the Grand Rounds Editor.

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Reduction of oral contraceptive dosage to the lowest effective levels is a well-accepted principle of conservative medical practice. In keeping with this view, Norinyl is now also available as Norinyl-1, containing exactly one half the previous dosage of norethindrone and mestranol. Clinical experience has established that effective fertility control can be achieved with the same degree of reliability and safety with new Norinyl-1 when taken as directed.

What about switching patients from higher dosage forms?

In transferring patients to low-dose Norinyl-1 from higher-dosage oral contraceptives, some breakthrough bleeding may occur in the early cycles. In the majority of cases the bleeding episode is mild and self-limited. The long-term advantages of the lower dosage form should be weighed against the inconvenience of possible breakthrough bleeding in the individual patient.

Prescribing Information

Contraindications: Patients with any symptoms or history of thrombophlebitis, pulmonary embolism, liver dysfunction or disease, carcinoma of breast or genital organs, or undiagnosed vaginal bleeding.

Warnings: Discontinue medication pending examination if there is sudden partial or complete loss of vision, proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. The safety of Norinyl-1 in pregnancy has not been demonstrated. If a patient misses two consecutive periods, pregnancy should be ruled out before continuing the medication. If she has not adhered to the prescribed schedule, pregnancy should be considered at the first missed period. Active ingredients of oral contraceptives have been detected in the milk of mothers who received these drugs; the significance to infants has not been determined.

Precautions: Pretreatment physical should include examination of the breasts and pelvic organs, as well as a Papanicolaou smear. If endocrine or liver function tests are abnormal during therapy, repeat tests are recommended after the drug has been withdrawn for two months. Following administration of drug, preexisting uterine fibromyomata may increase in size. Careful observation and caution are required for patients with symptoms or history of epilepsy, migraine, asthma, cardiac or renal dysfunction, cerebrovascular accident, psychic depression, and diabetes. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. Possible long-term effects of the drug on pituitary, ovarian, adrenal, hepatic or uterine function must await further studies. The physician should be alert to the earliest manifestations of thrombophlebitis and pulmonary embolism. The drug should be used judiciously in those young patients in whom bone growth is not complete. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask symptoms of the climacteric. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

Side Effects: The following have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals, mental depression. Although the following side effects have been reported in users of oral contraceptives, no cause and effect relationship has been established: anovulation posttreatment, premenstruallike syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, and itching. The following occurrences have been observed in users of oral contraceptives (a cause and effect relationship has neither been established nor disproved): thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory tests may be altered by the use of oral contraceptives: increased sulfobromophthalein and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in T^3 values), metyrapone test, pregnanediol determination.

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Here's why Norinyl-1 makes medical sense.

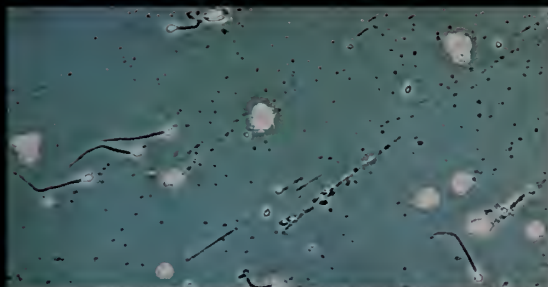
The effectiveness of Norinyl-1 as a low-dose oral contraceptive may be explained by its possible multiple action. In addition to its primary action of suppression of ovulation, Norinyl-1 may offer additional protective mechanisms... (1) creation of a cervical mucus that may be hostile to sperm penetration, and (2) development of an endometrium that may be out of phase with nidation.

These effects are illustrated below.

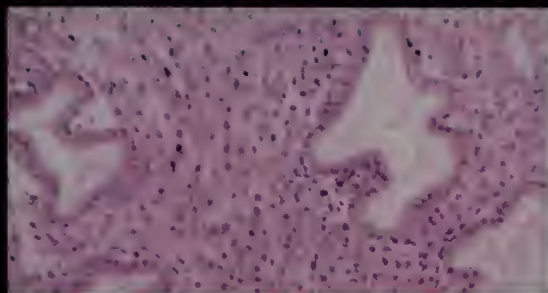
Untreated Patient



Cervical mucus at midcycle is usually thin and watery, with Spinnbarkeit (stretchability) of 15 to 20 cm.



Spermatozoa appear healthy, active, freemoving.

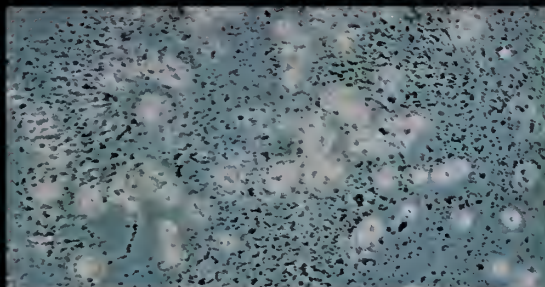


Endometrium of untreated patient is receptive to the fertilized ovum during secretory phase.

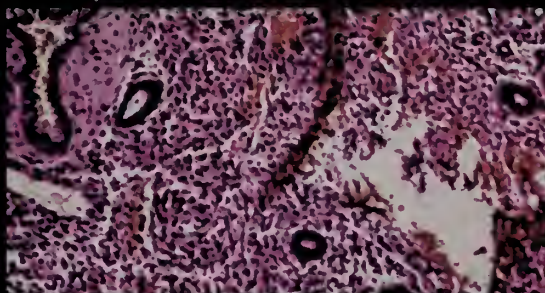
Norinyl-1 Patient



Cervical mucus at midcycle is scanty, viscous—with Spinnbarkeit of 1 cm. or less.



Immobile spermatozoa as they appear in cervical mucus taken from patient treated with Norinyl-1.



Norethindrone in Norinyl-1 accelerates secretory phase, suppresses glandular and vascular development.

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Turn page for contraindications, precautions and side effects.

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fluocinolone acetonide

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Product Information

Contraindications: Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components.

Precautions: Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for

prolonged periods of time. **Side Effects:** Side effects are uncommon with topical corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. In such cases the agent should be discontinued and appropriate measures taken.

Availability: Synalar (fluocinolone acetonide) Cream 0.025%—5, 15 and 60 Gm. tubes and 425 Gm. jars. Cream 0.01%—15, 45 and 60 Gm. tubes and 120 Gm. jars. Solution 0.01%—20 and 60 cc. plastic squeeze bottles. Ointment 0.025%—15 and 60 Gm. tubes. Neo-Synalar® (neomycin sulfate 0.5% [0.35% neomycin base], fluocinolone acetonide 0.025%) Cream—5, 15 and 60 Gm. tubes.

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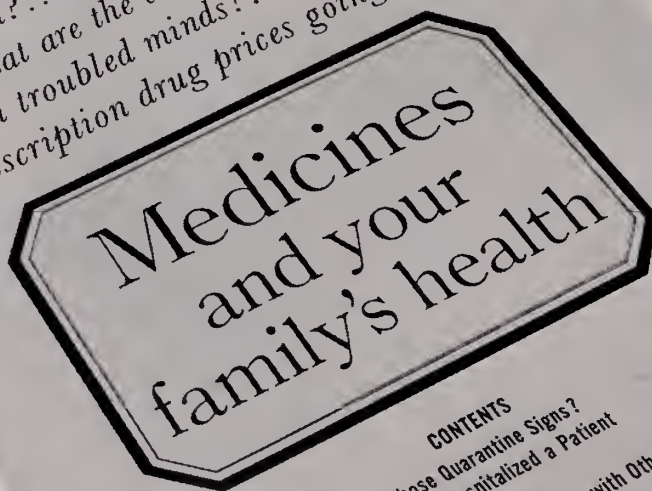
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vanished? ... What's in a drug name?
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What Ever Became of Those Quarantine Signs?
The Anonymous Drug That Hospitalized a Patient
Medicines for the Troubled Mind
How Does the Price of Medicine Compare with Other Prices?
Reprinted from the November, 1967 issue
of The Reader's Digest

2468



Abstracts, Briefs and Commentaries

ISOTOPES AS A DIAGNOSTIC TOOL*

The use of radioisotopes, or more properly radionuclides, as medical diagnostic agents, is undergoing a rapid evolution at the present time, particularly in the field of organ and tumor visualization. There is a growing appreciation of the array of complex factors which govern the retrieval of information from the various isotope distributions which occur in the body following the administration of radiopharmaceuticals. More sophisticated equipment, radiation sources which produce relatively little radiation dosage to the patient, and a variety of new radiopharmaceutical agents have given rise to an increase in available counting rates by a factor of a hundred or more in some cases. In particular the use of short-lived isotope generators, multiple head scanners and camera type detectors appears to be growing in many institutions. Future developments with spark chambers, avalanche chambers, image intensifiers and multiscanner configuration devices with sophisticated image-processing techniques developed to some extent in connection with space age projects hold much promise. The need for production of very short-lived radionuclides has led to the design and construction of small, relatively inexpensive reactors and cyclotrons for on-site use.

Paul V. Harper, M.D.**
Chicago, Illinois

*Presented at the Minnesota State Medical Association meeting in Duluth, May 15, 1967.

**Argonne Cancer Research Hospital and Department of Surgery, University of Chicago Hospitals and Clinics. Operated by the University of Chicago for the United States Atomic Energy Commission.

BELOW-KNEE AMPUTATION FOR ISCHEMIC GANGRENE

Fifty-five below-knee amputations were performed in 53 patients with far advanced ischemia of the lower extremity with a success rate of 83% in the 45 patients who survived the surgery. Twenty-eight of the 36 patients whose wounds healed successfully were rehabilitated with a prosthesis.

Important points in technique stressed by the authors were: (1) Circular skin incision to insure maximum chance for skin viability and (2) atraumatic handling of the tissue with guillotine division of the muscles.

The authors feel that if the profunda femoris artery is patent there will be sufficient collateral circulation to permit below-knee amputation. All of their

patients had good flow in the profunda femoris artery. They do not feel that flow through the superficial femoral and into the popliteal artery is necessary for a successful outcome.

Comment: The points in technique stressed in this article are commendable and it does seem reasonable that, with present day refinements in surgery, anaesthesia, and ancillary services, the risk of a second higher amputation should in a good many cases be taken in order to better rehabilitate a significant number of patients.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

Lim, Robert C., Jr. et al.: Below-Knee Amputation for Ischemic Gangrene. Surg Gynec Obstet 125:3:493, 1967.

LIMB SALVAGE IN DIABETICS WITH "HOPELESS ISCHEMIA"

The author reports on thirteen diabetic patients who underwent fifteen reconstructive vascular procedures to attempt salvage of limbs with extreme ischemia, eminent gangrene, or localized gangrene progressing towards "total tissue death." The common denominator for these cases was the tissue damage plus an extremely poor arterial runoff below the knee. One patient died post-operatively of a myocardial infarction. This patient was seventy-two years old and represents a mortality of 6.6%. Three of the remaining fourteen limbs subsequently required amputation.

Comment: This type of procedure can be done with as low a mortality as a limb amputation because, although the operating time is admittedly longer, the tissue disruption is much less. Reconstructive vascular procedures utilizing autogenous vein tissue and careful detailed technique can salvage limbs now which would have been amputated ten years ago. The sole question would seem to be whether the patient needs the limb for mobilization; for to salvage a limb that may still require special care in a bedridden patient on the basis of "morale boosting" hardly seems justified.

Harrison H. Farley, M.D.
Minneapolis, Minnesota

Alderman, O. B.: Limb Salvage in Diabetics with "Hopeless Ischemia." JAMA 201:4, 1967.

John Hunter as a Boy

A dullard at books, he knew more about ants, birds, bees, tadpoles, and worms than anyone in the neighborhood. He never tired of watching them, and to learn more about what they were like he cut them open. What he could not find by himself he tried to learn by questioning everyone: Why do leaves turn yellow and red in the autumn? Why do clouds take different shapes? What makes grass grow where it isn't planted? He would stop the farmhands at their work and ply them with questions: Why does milk dry up in the cow's udder when her calf is taken away? Why does a fierce bull become a docile ox after it is gelded? Not knowing the answers, nor even wanting to know, the farmers thought John a nuisance. And his parents were sure that no good could possibly come from this idle foolishness, which showed no signs of abating as he grew older.*

*Sarah R. Riedman: Masters of the Scalpel, 1962.



Book Reviews

Educate your children to self-control, to the habit of holding passion and prejudice, and evil tendencies subject to an upright and reasoning will, and you have done much to abolish misery from their future lives and crimes from society. Knowledge does not comprise all which is contained in the large term of education. The feelings are to be disciplined; the passions are to be restrained; true and worthy motives are to be inspired; a profound religious feeling is to be instilled, and pure morality inculcated under all circumstances. All this is comprised in education.—Daniel Webster.

THE THYMUS: EXPERIMENTAL AND CLINICAL STUDIES—A Ciba Medical Foundation Symposium. G. E. W. Wolstenholme and Ruth Porter, editors. Little Brown and Company, Boston, Massachusetts, 1966, 538 pages, \$15.00.

This book represents a collection of papers read at a symposium in Melbourne, Australia, on August 25 through 27, 1965, in honor of Sir Macfarlane Burnet. It includes monographs in the general fields of (1) the structure and development of the thymus, (2) the function of the lymphocyte, (3) the role of the thymus and cellular and humoral immunity, (4) the role of the thymus in leukemogenesis and carcinogenesis, and (5) auto-immune disease of the thymus: experimental and clinical studies. Most papers are followed by discussions. Illustrations and references are adequate.

The participants in this international symposium included many of the well recognized scholars in the field of immunology, and consequently most of the papers presented are quite detailed. This book will be of considerable interest to the physician primarily interested in immunology but will probably not be of much use to the practicing physician.

Gerald Onstad, M.D.
Hennepin County General Hospital

DERMATOPATHOLOGY, by Hamilton Montgomery, 1320 pp., 1777 illustrations (58 in color), \$60, New York, Hoeber Medical Division, Harper & Row, 1967.

Rarely out of the maw of the medical press comes a classic. When I call *Dermatopathology* a classic, I mean it is an authoritative work of such excellence that it will endure.

Hamilton Montgomery, emeritus consultant and emeritus professor in the section of dermatopathology at the Mayo Clinic, has studied the skin since 1918. He leaned toward skin diseases naturally, for his father was a dermatologist. With Ormsby, the older Montgomery wrote *Diseases of the Skin*, a well-known textbook now

in its eighth edition. Eventually the son replaced his father as that book's coauthor and went on to become an international authority in his field.

He prefaces his book with the remark that he put it together for "those who are interested in dermatopathology in its broadest aspects." This audience, he adds, includes not only dermatologists and pathologists, but clinicians who want to understand skin changes in systemic disease, research workers who seek investigative details, and students who wish to ground themselves in fundamentals of dermatology.

Doctor Montgomery prescribes a tall order for himself. How does he carry it out? After he introduces the book and gives a chapter on biopsy, he has his colleague, Richard K. Winkleman, a professor of dermatology, write two sections—Histochemistry of the Skin and Normal Structure of the Skin. Once Doctor Winkleman tells what skin is and how to prepare and stain it, Doctor Montgomery proceeds with the next 34 chapters.

To portray the contents briefly is difficult. Chapters begin with congenital dysplasias and end with metastatic cutaneous neoplasms. Between these extremes, the author describes and illustrates about everything that can happen to the skin. With each lesion or group of lesions he defines terms, sketches historical background, clarifies pathological features, and sets forth relevant facts on diagnosis and pathogenesis. He writes clearly and, when he discusses controversial topics, he does not hesitate to tell where he stands.

While Doctor Montgomery's discussions are excellent, what distinguishes *Dermatopathology* are its 1777 illustrations. He has assembled a vivid array of photomicrographs, and his 58 color plates are among the best I have seen. Readers who know the expense of colored reproductions will appreciate why the book costs \$60. This handsomely bound and beautifully produced two-volume set will occupy a prominent place in the libraries of dermatologists and pathologists.

Richard L. Reece, M.D.
Minneapolis, Minnesota



"George wants to know if it's okay to take his cold medicine now, Doctor, instead of seven o'clock?"



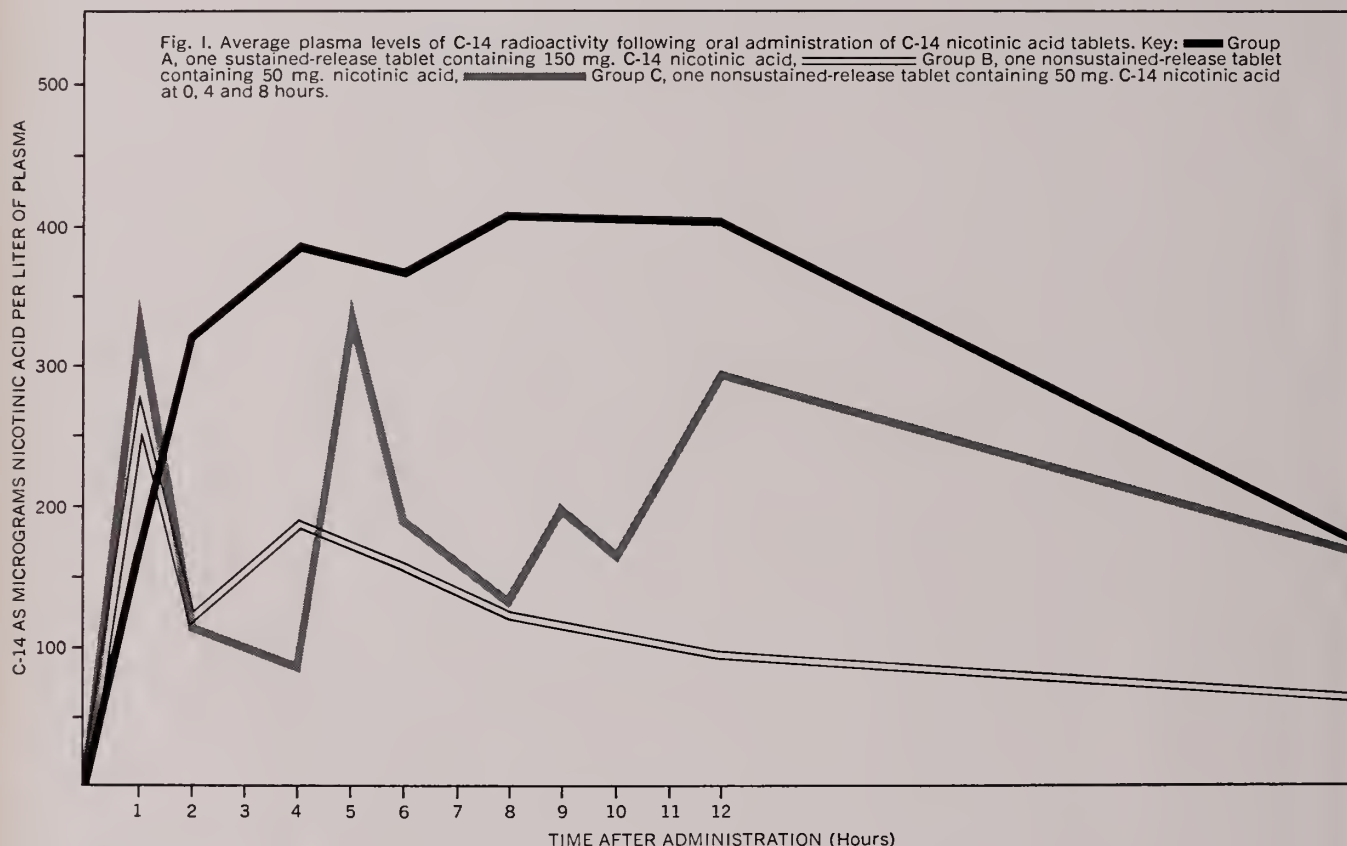
The long-continued action of Novahistine LP should help you both get a good night's sleep. Two tablets in the morning and two in the evening will usually provide round-the-clock relief by helping clear congested air passages for freer breathing. Novahistine LP also helps restore normal mucus secretion and ciliary activity—normal physiologic defenses against infection of the respiratory tract. Use cautiously in individuals with severe hypertension, diabetes mellitus, hyperthyroidism or urinary retention. Caution ambulatory patients that drowsiness may result. Each Novahistine LP tablet contains: phenylephrine hydrochloride, 25 mg., and chlorpheniramine maleate, 4 mg.

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Human volunteer subjects were administered Geroniazol TT tablets with the nicotinic acid component made radioactive with C-14. Plasma and urine samples were analyzed. (See Figures I and II) The radioactive tracer study substantiated the previous clinical evidence that the release of nicotinic acid from the Geroniazol TT tablet produced a gradual rise in plasma levels to a plateau for a total of 12 hours and more.

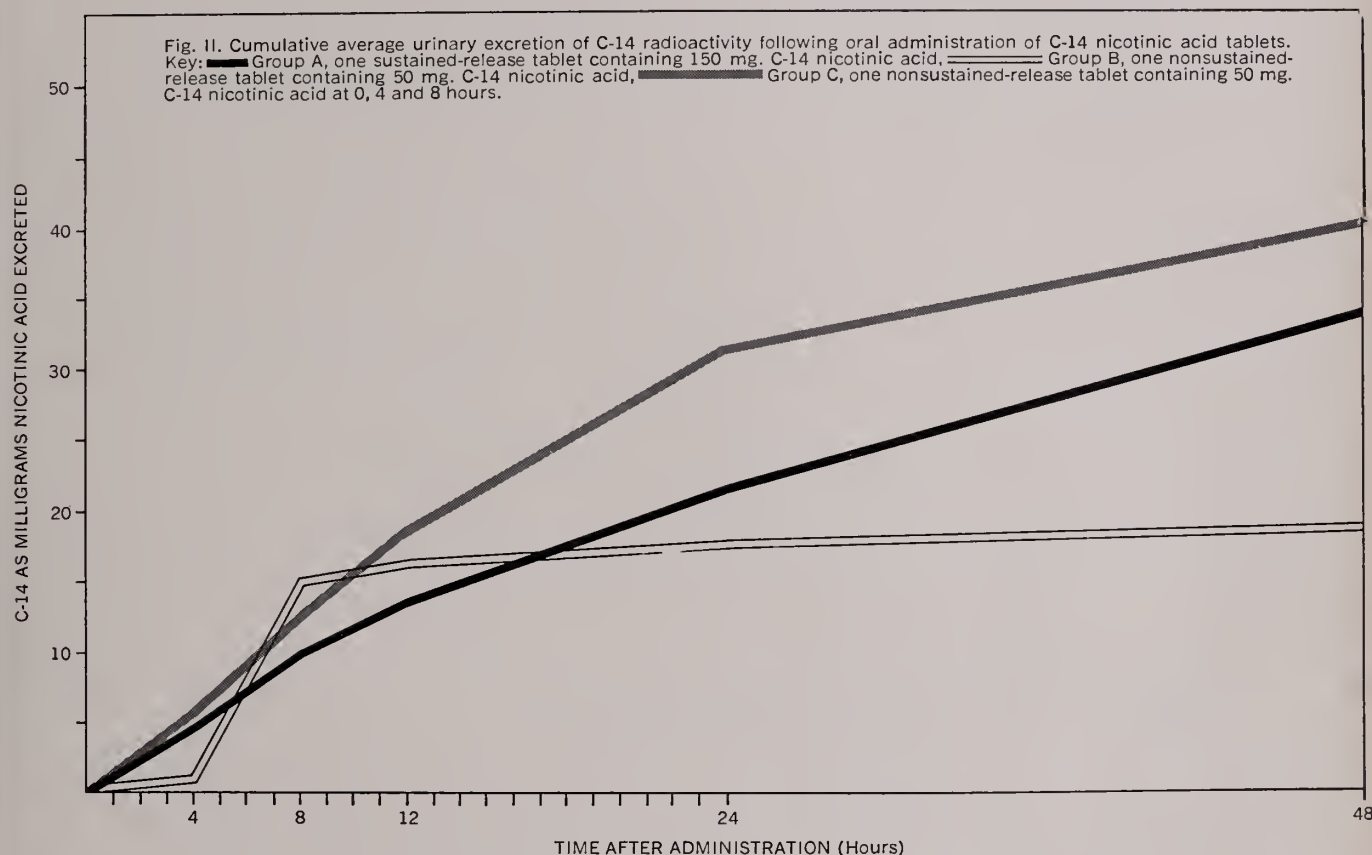
Such proven sustained activity makes the management of geriatric patients much easier by minimizing the possibility of neglected doses through absent-

mindedness or senile confusion. Therapy *can* be continuous on a daily dose of only one Geroniazol TT tablet every 12 hours.

The gradual release of nicotinic acid in Geroniazol TT will provide the well-known peripheral vasodilation needed in patients with deficient circulation and with a minimum amount (if any) of "flushing." Also, cerebrovascular circulation is complemented by pentylentetrazol, long-established as a cerebral and respiratory stimulant.

Geroniazol TT improves the typical, unfortunate, signs of senile confusion. Patients become more alert,

aged and debilitated



less confused and moody. Personal care, memory, emotional stability, social attention improve. Fatigue, apathy and irritability are reduced.

A prescription for 100 tablets of Geroniazol TT will permit your patients to enjoy the benefits of time-prolonged nicotinic acid/pentylentetrazol therapy, at an economical price. Dosage is only one tablet every 12 hours.

Contraindications: There are no known contraindications.

Precautions: Exercise caution when treating patients with a low convulsive threshold.

Side Effects: Side effects are rarely encountered, however due to the vasodilatation effect of nicotinic acid, transitory mild nausea, flushing, tingling and pruritus are possible.

Dosage: One tablet every 12 hours.

Supplied: Prescribe bottles of 100 tablets, to take advantage of recent price reduction.

References: 1. Report by Nuclear Science & Engineering Corp., Pittsburgh, Pa., in files of Philips Roxane Laboratories. 2. Connolly, R.: W. Virginia Med. J. 56:263 (Aug.) 1960. 3. Curran, T. R., and Phelps, D. K.: Am. Pract. & Digest Treat. 11:617 (July) 1960.



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Special Article

Serum Creatine Phosphokinase as a Diagnostic Aid

A

Review*

DANIEL J. LOEGERING, M.A.**
JERRY B. CRITZ, Ph.D.**
JEAMES A. WAGNER, M.A.**

London, Ontario

SERUM ENZYMES have now been used for years to diagnose diseases. Serum creatine phosphokinase is one of these enzymes, but it was not introduced into the United States until 1962.¹

Creatine phosphokinase catalyzes the reversible transfer of a high energy phosphate group from adenosine triphosphate to creatine as follows:



The reaction can be made to proceed in either direction by adding appropriate substrates. Creatine phosphate hydrolyzes to creatine and inorganic phosphate, and the phosphate is then measured colorimetrically.² If the reverse reaction is used, creatine is determined, also with a colorimeter.^{3,4}

Some feel assays of inorganic phosphate and creatine are not as reliable as techniques which measure adenosine diphosphate or adenosine triphosphate.⁵ However, determinations of these are more difficult because they link adenosine triphosphate and adenosine diphosphate to secondary enzyme systems which convert DPNH to DPN or TPNH to TPNH. The change of optical density in the reaction systems determines the activity of creatine phosphokinase.^{6,7}

Creatine phosphokinase is an excellent enzyme for testing because of its distribution. It is concentrated in skeletal and heart muscle and, to a lesser extent, in brain tissue. It cannot be detected in red cells, liver, or kidney.⁸ Because of this distribution, an increase in serum creatine phosphokinase usually indicates skeletal muscle or heart damage, and lack of activity eliminates in red blood cells the problem of hemolysis (Table 1).⁹

Muscular Dystrophy

Patients with muscular dystrophy have ele-

*Supported in part by Grant AM 06154, National Institute of Health, USPHS.

**The Department of Physiology, University of Western Ontario Faculty of Medicine, London, Ontario, Canada.

vated levels of several enzymes. These include aldolase,¹⁰ the transaminases,^{11,12} lactic dehydrogenase, and malate dehydrogenase. In 1959 Ebashi and his coworkers discovered that patients with progressive muscular dystrophy also had elevated serum creatine phosphokinase.¹³ Studies also showed that serum creatine phosphokinase surpassed other enzymes in diagnosing dystrophy¹⁴ and also helped to separate the Duchenne type of dystrophy from other forms.¹⁵

TABLE 1
Human Tissue CPK and GOT Activity

CPK* ¹⁰		GOT** ¹¹	
Tissue		Tissue	
Skeletal muscle	18,400	Heart	7,800
Heart	5,540	Liver	7,100
Brain	3,400	Skeletal muscle	5,000
Adrenal gland	136	Kidney	4,500
Lung	0.5	Pancreas	1,400
Liver	0	Spleen	700
Prostate	0	Lung	500
Red blood cell	0	Red blood cell	15
Serum	0	Serum	1

*Mean activity of soluble protein, International units (X10⁴)/mg.

**Relative activity referred to serum as unity.

The Duchenne type, the most severe, causes the greatest rise in serum creatine phosphokinase;¹⁷ and younger patients, who have had the disease for the shortest time, show the highest levels. In other inherited myopathies, the enzyme goes up, but much less than in patients with the Duchenne type. In the dystrophies, severity of the disease correlates well with serum creatine phosphokinase levels (Table 2).¹⁶ Furthermore, levels increase in preclinical cases of Duchenne dystrophy, especially in young patients with a family history of dystrophy.¹⁸

TABLE 2
Serum CPK Activity in Different Types of Muscular Dystrophy

Type	Mean SCPK ¹⁶
Duchenne type	373 I.U.
Lim-girdle type	26 I.U.
Fascioscapulohumeral type	10 I.U.
Upper limit of normal	3.5 I.U.

The age at which the sample is taken must be kept in mind, for serum creatine phosphokinase decreases as patients with Duchenne's dystrophy grow older (Figure 1).^{16,19} Duchenne dystrophy could be diagnosed as the limb-girdle type if the patient is not tested at the

proper time. Enzyme decrease may be due to loss of functional muscle mass;^{16,19} but Stephens and Lewin report that decrease of serum enzyme activity may be due to the lack of activity of the patient as the disease reaches its final stages.²⁰

Acquired Myopathies

Acquired myopathies or muscular atrophy of neurogenic origin seldom cause a rise in serum creatine phosphokinase. Dermatomyositis,⁸ polymyositis,¹⁶ and denervation¹⁹ occasionally produce elevation; but poliomyelitis, polynuritis, myasthenia gravis,²¹ anterior horn diseases, and peripheral nerve diseases⁸ do not.

Duchenne Muscular Dystrophy Carriers

Some carriers of Duchenne dystrophy have elevated serum creatine phosphokinase. Studies indicate that 70 to 80 percent of known carriers have levels of one to four times normal.^{18,22,23} Known carriers are those with a family history of dystrophy and are parents of dystrophic children. Creatine phosphokinase values vary in these carriers, but they are more consistently increased than with other serum enzymes. Brugsch and his associates were unable to detect carriers with lactic dehydrogenase, glutamic-oxalacetic transaminase, and glutamic-pyruvic transaminase tests, although a few carriers showed elevated serum aldolase.²⁴ Pearce, Pennington, and Walton tested female relatives of patients with Duchenne dystrophy and concluded that serum creatine phosphokinase offered a sound basis for genetic counseling.¹⁸ Carriers apparently have isolated dystrophic muscle fibers, which may be responsible for the elevated serum creatine phosphokinase. These fibers later disappear, giving normal levels even in known carriers.²⁰

Stephens and Lewin say that physically active carriers may have higher enzyme levels.²⁰ In four carriers, 10 hours of bed rest reduced serum creatine phosphokinase to normal; yet when they exercised, enzyme activity rose promptly. This phenomenon did not occur in normal subjects. The authors suggested that the enzyme leaked through the abnormal muscle membrane when carriers exercised.²⁰

Myocardial Infarction

Because creatine phosphokinase is concen-

trated in the myocardium, serum levels rise when heart damage occurs. Dreyfus *et al.* first illustrated this in 1960,⁴⁹ and many have since confirmed it. Precisely what per cent of patients with known infarcts have elevated serum creatine phosphokinases remains unknown. But to date almost all patients tested have shown an increase. Of 93 patients reported in two studies,^{26,27} only one failed to have an increase after an infarction.

Serum creatine phosphokinase and glutamic-oxalacetic transaminase remain high for about the same time span after an infarction. Both first increase about six hours after symptoms start, peak at 24 to 48 hours, and return to normal after three or four days (Figure 2)²⁷⁻³⁰. Creatine phosphokinase increases relatively more than transaminase. While transaminase may go up to 12 times its normal level, creatine phosphokinase can exceed 40 times its usual range.

Whether peak values of serum creatine phosphokinase can be used to forecast prognosis or whether they reflect the size of infarcts is not yet certain. However, Sorenson found that patients who had high creatine phosphokinases at 48 hours fared more poorly than patients whose phosphokinase returned to normal in that time¹⁶; and Muller ligated coronary arteries in dogs, measured the infarct size, and found that serum creatine phosphokinase correlated well with the extent of necrosis.³⁰

Compared to other serum enzyme tests which increase in myocardial necrosis, creatine phosphokinase is more specific. In a patient with typical symptoms of infarction, Warburton *et al.* go so far as to say that an elevated level 48 to 72 hours after the attack is diagnostic of myocardial infarction.²⁸ It is superior to serum glutamic oxalacetic transaminase and aldolase because these relatively nonspecific enzymes may rise in shock, probably because of slight liver necrosis²⁹. In terms of specificity, serum creatine phosphokinase compares well even with lactic dehydrogenase isozymes. Alpha-hydroxybutyric dehydrogenase, an isozyme of lactic dehydrogenase specific for heart muscle, is not wholly satisfactory for diagnosing infarction. Lactic dehydrogenase isozymes can yield similar or identical patterns in patients with myocardial infarction, infarcts of the kidney, pernicious anemia, lymphomas with

hemolytic anemias, or progressive muscular dystrophy³¹.

Cerebral Infarction

Brain tissue has a creatine phosphokinase concentration slightly more than half that of heart muscle. Acheson has reported that 15 to 24 patients with acute cerebrovascular accidents

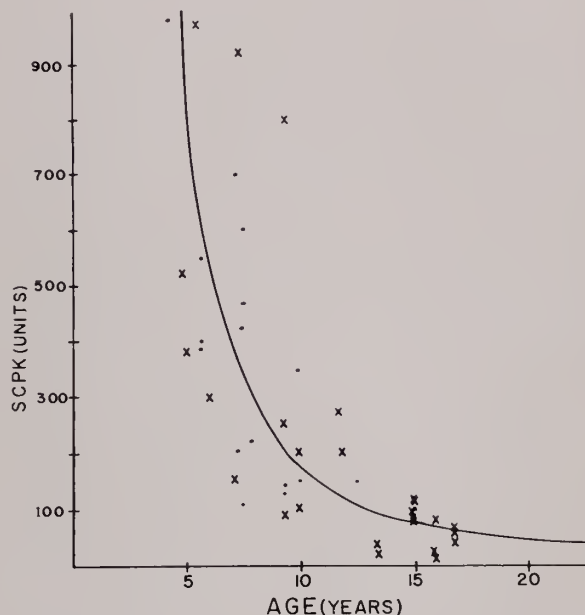


Fig. 1—The relation between serum levels of creatine phosphokinase and the age of patients with the Duchenne type of muscular dystrophy. (From Pearce, Pennington, and Walton, 1964¹⁷; and Hughes, 1963²⁰.)

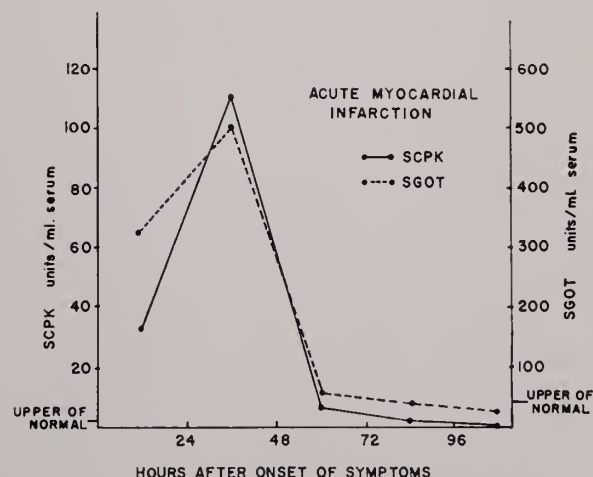


Fig. 2—The time course of serum creatine phosphokinase and serum glutamic oxalacetic transaminase activity of a single patient with a severe acute myocardial infarction. The upper limit of the normal range for each enzyme is indicated on the ordinate by ULN. (From Vincent and Rapport, 1965²⁸.)

had elevated serum levels.³² Levels peaked in four days and returned to normal in eight days. Four of the five patients who died had levels seven times normal. Thus, in patients who died, the higher the level, the worse the prognosis. In those who survived, the level apparently had little to do with the severity of brain damage.

Other Diseases

Since creatine phosphokinase is absent from the liver, it does not rise in liver disease. This is perhaps its greatest advantage over other enzyme tests. In fact, when used with other enzymes, its very absence can help pinpoint the liver as a source of trouble. For example, in congestive failure, as the liver becomes congested, transaminase levels will climb, but serum creatine phosphokinase remains normal.²⁹

Muscle trauma, including surgery, will increase creatine phosphokinase activity. The level depends on the extent of injury. A two to five-fold increase was found 24 hours after major surgery in five patients, but a single patient with basal cell carcinomas who had them excised had no rise.²⁴ Frequent intramuscular injections of irritating drugs, such as aqueous penicillin, can elevate creatine phosphokinase four to five times, but occasional injections of narcotics, diuretics and barbiturates do not appear to influence the level.¹ Patients with hemorrhagic pancreatitis involving the abdominal muscles also have high levels.³⁴

Because creatine phosphokinase is specific for myocardial necrosis, it can be used to exclude other diseases with similar symptoms. Myocarditis may mildly increase serum creatine phosphokinase, but only if it produces ischemic necrosis.²⁹ Angina pectoris,³⁵ pericarditis,²⁹ coronary insufficiency, cardiac arrhythmia,²⁷ tachycardia, and arteriosclerotic hypertensive heart disease²⁶ usually show normal levels.

Pulmonary embolism or pulmonary infarction do not generally boost serum creatine phosphokinase levels.^{26,27} However, Velez-Garica *et al.*, using Fiske and Subbarow's method, found that 13 of 33 patients with pulmonary disease showed increased phosphokinases. None of these patients had electrocardiographic evidence of myocardial infarction; but

the 13 with increased levels all had severe acute pulmonary disease. The authors felt that damaged lung tissue might release the enzyme, but they added that anoxic or edematous skeletal muscle was a more likely source. Velez-Garica and his associates also point out that patients with diabetic acidosis and intoxicated chronic alcoholics have increased levels.³⁴

Hypothyroidism

In hypothyroidism, serum creatine phosphokinase values may go up two to five times normal. When patients are treated, the level returns to normal in three to four weeks and remains normal as long as the patients are euthyroid. No one has explained this satisfactorily, though many have commented on it.³⁶⁻³⁹

Non-Disease States

Generally, only prolonged exercise will increase serum levels. Short-term exercise has no effect: for example, rapidly climbing 70 stairs or a brisk four-mile walk.^{23,40} A two-hour run will cause a three-fold increase, a 25-mile walk a seven-fold increase, and a 53-mile walk a 24-fold increase.^{40,41} Intense physical labor for two days will also result in a rise.⁴¹ In our laboratory a large number of dogs running on a treadmill at 10 miles per hour for one hour demonstrated a large increase in serum creatine phosphokinase activity (43 Im U/ml increased to 250 Im U/ml, unpublished dissertation). Griffiths found that the normal range of creatine phosphokinase differs in active and resting people.⁴¹ Rat studies support this. Kindrick-Jones and Perry report that confined rats had creatine phosphokinase activities lower (283 units) than non-confined control rats (497 units).⁴³

During pregnancy, serum creatine phosphokinase remains stable.^{37,43} At delivery and for one to two days after, enzyme levels increase up to three times normal.^{44,45} This is believed to be due to loss of creatine phosphokinase from the uterus as it involutes.^{44,46} According to Emery and Pascasio, the involuting uterus loses 3300 units of enzyme during the first two postpartum days.⁴⁴

Reports vary concerning the effect of age and sex on the serum level of creatine phosphokinase. Newborns have a serum level two

to three times adult levels, and it remains elevated for from one to ten years.^{40,48} Then the level remains constant through adult life. Men and women differ little in their creatine phosphokinase levels although some investigators report a slightly higher level in men.⁴⁹

Summary

Creatine phosphokinase, an enzyme concentrated mostly in the myocardium and in skeletal muscle, increases in the serum when dystrophy or myocardial infarction occurs. In dystrophy, levels are especially high early in

the disease and descend as the disease progresses and muscle mass is destroyed. Carriers of the disease tend to have higher levels than normal. For diagnosing myocardial infarction, the enzyme may be better than the serum glutamic-oxalacetic transaminase. It reaches relatively higher levels and, because of its absence from the liver, does not increase with liver congestion as the transaminase sometimes does. Other conditions which can cause serum creatine phosphokinase elevations include cerebral infarction, hypothyroidism, violent exercise, major surgery, and involution of the uterus after delivery.

References

1. Hess, J. W., and MacDonald, R. P.: Serum Creatine Phosphokinase Activity. A New Diagnostic Aid in Myocardial and Skeletal Muscle Disease. *J Mich Med Soc* 62:1095, 1963.
2. Fiske, C. H., and Subbarow, V.: The Colorimetric Determination of Phosphorus. *J Biol Chem* 66:375, 1925.
3. Ennor, A. H., and Rosenberg, H.: Some Properties of Creatine Phosphokinase. *J Biochem* 57:203, 1954.
4. Eggleston, P., Elsdon, S. R., and Gough, N.: The Estimation of Creatine and of Diacetyl. *Biochem J* 37:526, 1943.
5. Preston, J. A., Batsakis, J. G., Briere, R. O., and Taylor, R. V.: Serum Creatine Phosphokinase. A Clinical and Laboratory Evaluation. *Amer J Clin Path* 44:71, 1965.
6. Tanzer, M. G., and Gilvarg, C.: Creatine and Creatine Kinase Measurement. *J Biol Chem* 234:3201, 1959.
7. Nielsen, L., and Ludvigsen, B.: Improved Method for Determination of Creatine Kinase. *J Lab Clin Med* 62:159, 1963.
8. Hess, J. W., MacDonald, R. P., Frederick, R. J., Jones, R. N., Nely, J., and Gross, D.: Serum Creatine Phosphokinase (CPK) Activity in Disorders of Heart and Skeletal Muscle. *Ann Intern Med* 61:1015, 1964.
9. King, J.: *Practical Clinical Enzymology*. London. D. Van Nostrand Co., Ltd., p. 123, 1965.
10. Thompson, R. A., and Vignos, P. J.: Serum Aldolase in Muscle Disease. *Arch Intern Med* 103:155, 1959.
- 11-48 May be secured from the author or the reprints.

Irido-Diagnosis

The poetical notion that the eye is the mirror of the soul evidently convinced a minor medical prophet in Chicago that money might be made by founding a school of medicine in which the diagnosis of all diseases would depend on the ability to notice the changing colors of the iris or colored material of the eye. With a remarkable genius for publicity, he succeeded in attracting much free newspaper mention and in leading to his school numerous ignorant satellites who desired to enter on the practice of healing by some easy route. Among those attracted have been a few regularly licensed physicians who sought to exploit themselves and enhance their incomes by adding the claim of this superior power to such as might already have been conferred upon them by the state. Even today the practitioners of this vagary burst into temporary luminescence in the sensation-seeking press. Fortunately the prophet himself was accused by his wife of mental vagaries. He gradually subsided!*

*Morris Fishbein, M.D.: *New Medical Follies*, 1927.

Man should go out of this world as he came in—chiefly on milk.

—William Osler



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so smoothly that patients are often untroubled
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*15 mg. of Butisol (butabarbital), plus the other ingredients, in outer layer; 15 mg. of Butisol (butabarbital) in a specially coated core for delayed action, to approximately equalize duration of action for all components.

Contraindicated in presence of renal impairment, peptic ulcer, ulcerative colitis, or mental depression, and in patients with porphyria or those sensitive to any component. **Warning:** Coated potassium tablets, sometimes administered in conjunction with anti-hypertensive therapy, may be associated with small bowel lesions which have led to obstruction hemorrhage, and perforation. Surgery has been required and deaths have occurred. Such tablets should be used only when indicated and when adequate dietary supplementation is not practical. They should be discontinued immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occur. **Precautions:** Exercise caution in hepatic disease, diabetes, surgery, coronary artery disease, epilepsy, E.S.T., and in patients receiving digitalis. **Side Effects:** Electrolyte imbalance, hyponatremia, hypochloremic alkalosis and/or hypokalemia, hyper-

uricemia and gout, bradycardia, drowsiness, skin rashes, hangover, systemic disturbances, weakness, leg cramps, diarrhea, epistaxis, dizziness, urticaria, dry itching skin, nausea, vomiting, palpitation, superficial skin bruises, headache, dehydration, paresthesias, photosensitivity, pancreatitis, jaundice, xanthopsia, thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, nasal congestion, hypotension, lassitude, loose stools, anorexia, bizarre dreams, peptic ulcer, ulcerative colitis, mental depression. (Ammonium chloride, which may be administered to reverse hypochloremic alkalosis, should not be given to patients with hepatic disease.) **Before prescribing or administering, see package insert.** †Warning: May be habit forming. **Usual Adult Dosage:** Butiserpazide®-25 or Butiserpazide®-50: 1 tablet daily or b.i.d. **References:** 1. Johnson, H. J., Jr.: *Penna. M. J.*: 67:35, 1964. 2. Coodley, E. L.: *Curr. Ther. Res.* 4:460, 1962.

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Indications: Urinary tract infections caused by gram-negative and some gram-positive organisms.

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Precautions: As with all new drugs, blood and liver function tests are advisable during prolonged treatment. Pending further experience, like most chemotherapeutic agents, this drug should not be given in the first trimester of pregnancy. It must be used cautiously in patients with liver disease or severe impairment of kidney function. Because photosensitivity reactions have occurred in a small number of cases, patients should be cautioned to avoid unnecessary exposure to direct sunlight while receiving NegGram, and if a reaction occurs, therapy should be discontinued. The dosage recommended for adults and children should not arbitrarily be doubled unless under the careful supervision of a physician. Bacterial resistance may develop.

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Dosage: Adults: Four Gm. daily by mouth (2 Caplets® of 500 mg. four times daily) for one to two weeks. Thereafter, if prolonged treatment is indicated, the dosage may be reduced to two Gm. daily. Children may be given approximately 25 mg. per pound of body weight per day, administered in divided doses. The dosage recommended above for adults and children should not arbitrarily be doubled unless under the careful supervision of a physician. Until further experience is gained, infants under 1 month should not be treated with the drug.

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References: (1) Based on 23 clinical papers, 1512 cases. Bibliography on request. (2) Bush, I. M., Orkin, L. A., and Winter, J. W., in Sylvester, J. C.: Antimicrobial Agents and Chemotherapy—1964, Ann Arbor, American Society for Microbiology, 1965, p. 722.

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*As many as 9 out of 10 urinary tract infections are now caused by gram-negative organisms: E. coli, Klebsiella, Aerobacter, Proteus, Paracolon or Pseudomonas?... However, infections of the urethra and prostate caused by non-gonococcal gram-negative organisms are believed to be less prevalent.

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Law and Medicine

The "Police Hold"—A Benevolent Abuse

ALMOST DAILY the police bring a person to the psychiatric ward of the county general hospital in Minneapolis or Saint Paul, leaving him in the hands of hospital personnel with "Police Hold" stamped somewhere on the chart or order book. The police do not themselves place the stamp there. Hospital personnel do—in the widely accepted belief that they are executing a valid police power.

Stamping the Record

From the point of view of the police the practice probably stems from so stamping the record of a prisoner in a jail or penitentiary, the prisoner upon expiration of his sentence being then held to answer a further criminal charge. The distinction here is that the hospital is not a place of detention to which the criminally accused has been lawfully committed in the first instance; it is a place to which a prisoner might be sent for evaluation or treatment by a court of competent authority. That is precisely the flaw in the practice of "Police Hold": it is the exercise, by the executive, of a power belonging to the judiciary; the power to commit.

The police have the power to detain a criminally accused person for a reasonable time, until he can be brought before a magistrate for a preliminary hearing.

The place of detention is usually specified by statute as the city jail or the like:

"If . . . arrest be made on Sunday or after sunset or before 9:00 a.m. of any day, then the person . . . arrested should be confined in the City jail, or such other secure place as may be provided or obtained . . . until 9:00 a.m. next following such arrest . . . for hearing . . . "*.

Presumably the County Hospital is a secure place for certain persons. But any detention of the prisoner-now-patient beyond the maximum statutory (and constitutional) period (24 hours) would be a false imprisonment for which participating hospital personnel could be liable.

In Minneapolis the police have become skilled in spotting psychiatric cases. Usually it is psychotic individuals who are brought to the General Hospital for some minor infringement of the law: simple assault or disorderly conduct and occasionally for a felony such as burglary. A "Police Hold" is "put" on the prisoner/patient by rubber stamp. If the charge is sufficiently serious, the police return on a subsequent day to take the accused for further criminal processing, but more often the police never return for the prisoner/patient. He thereupon molts his prisoner status and becomes a patient. Later the supervisory staff agonizes over releasing him without first checking to see whether the police still want him.

*Chapter 630.050 of the Minneapolis Code of Ordinances.

The Saint Paul Ordinances contain no provisions comparable to those of Minneapolis. This is of small significance because it matters little legally where the accused is detained so long as there is no infringement of his constitutional safeguards; these include the right to have counsel present at interrogation*, the right to be warned prior to being questioned**, the right to have counsel present when identified as a suspect†, and other rights.

The Solution

Hospital personnel who actively abet the police in violating any of these rights could conceivably be liable for conspiracy to interfere with civil rights‡ apart from action for false imprisonment or false arrest.

The technically correct procedure is for the police to fetch the prisoner at the hospital and bring him before a magistrate within the statutory time provided; the magistrate then may commit the defendant to the hospital until his next court appearance (or discharge him absolutely if not committing him to jail).

In a sense the police by this practice are using an arrest lawful in its inception to effect a civil commitment, in that they thus compel the mentally-ill individual to become an involuntary psychiatric patient. Generally this has a salutary effect: the patient, often psychotic at the time of his arrest, is prevented from harming himself or others and is brought to treatment; often chemotherapy promptly produces a remission. A humane advantage here to the credit of the police is that a plainly psychotic person is spared a purely formal criminal process which would probably end in dismissal or acquittal, and he is protected and treated medically.

The disadvantages of thus cutting off legal corners should be evident from the foregoing. The safe course for hospital personnel to follow is never to honor a "Police Hold" beyond the statutory time limit for preliminary hearing. Should the prisoner/patient demand his release thereafter, it must be granted him forthwith unless civil commitment has been effected or some principle of law like the doctrine of medical emergency permits detaining him.§

Barlow Smith, LL.B., M.D. #
Minneapolis, Minnesota

**Escobedo v. Illinois*, 378 U.S. 478, 84 S. Ct. 1758, 12 L. ed. (2d) 977.

***Miranda v. Arizona*, 387 U.S. 436, 86 S. Ct. 1602, 16 L. ed. (2d) 694.

†*U. S. v. Wade*, U. S., 87 S. Ct. 1926.

‡Under 42 U.S.C.A. §1985.

§Here desperate hospital personnel are prone to seek the bastard ally of the "Police Hold," namely, the "Administrative Hold," a shibboleth by which many a false imprisonment has been sanctioned. This consists of securing the approval of a layman in the hospital administration to detain the patient. Where the responsible physician lacks the right to detain a patient, a lay person cannot confer that right upon him: this too would be an arrogation of the judicial power to commit.

#New York Bar, the District of Columbia Bar and the Minnesota Bar.

Snobs talk as if they had begotten their own ancestors.

—Herbert Agar

Come now, and let us reason together . . .

—Isiah 1

How vain it is to sit down to write when you have not stood up to live.

—Thoreau

Medicine and Religion

Dying^{*}

SOMEONE HAS said, "Nothing really happens until it happens to you." We read of accidents, losses, suffering, and death, but not until the news item applies to us or our immediate families do we fully understand the emotional shock, the spinning of the mind, and the spiritual strain that comes from a painful, sad experience. "The world looks different to me now," said a young man who had received the verdict of six months to live.

Articles and books have been written and lectures and sermons given on how to face death; yet, when all is said and written, no two people are alike and therefore no fixed procedure can be followed. In all such circumstances the family involved must be considered and also the personalities of the doctors and spiritual advisors. Generally speaking the following can be said:

Spiritual House in Order

Sick or well, a man should keep his house in order. Sudden death can come to a man at any age. A sense of accountability to God and man counsels all of us to see that those who remain after our departure are provided for materially and spiritually—materially, within the range of one's income; spiritually, by living a life of humble obedience to God, usefulness to one's fellowmen and maintaining a disposition that gives a lift to the heart of those who sorrow. The memory of a noble life is, in the long run, the greatest comfort to those who mourn.

To Tell or Not to Tell

The authority to tell a patient he suffers from an incurable disease rests with the family. They will, of course, seek counsel from the doctor and spiritual advisor. If a good rapport has existed before facing the problem of "to tell or not to tell," the decision arrived at will come from love and understanding and will be the right one, to the degree to which we humans can be right.

The acceptance of imminent death, though requiring a painful adjustment, can be and often is fruitful in bringing about a closer bond of affection in the family. This deeper relationship will give to all concerned strength of character and peace of mind which will linger long after death brings separation.

Hope

Hope need never be abandoned! Hope built on wishful thinking or religion as magic will collapse and cast a shadow across the sick and troubled relatives. Hope built on the 23rd Psalm or the 14th chapter of John (which takes in

^{*}Presented at the Annual Meeting of the Minnesota State Medical Association, May 15, 1967.

the whole of life, now and hereafter) puts eternity in the background and places both joy and sorrow in their proper relationship.

Belief in God

When religion has consisted mostly of intellectual assent to a creed, loyalty to an institution, or emotionalism, the facing of death is a severe strain on belief in the goodness of God. Where a man's religion has played a vital part in every department of his life—his home, occupation, friendships and pleasures—he has resources to meet the unexpected as though it were the expected, including death.

Turn to another associated question: "Should life be prolonged by mechanical means when there is no hope of recovery and the patient is in severe pain, unconscious, and reduced to a 'vegetable'?"

It is assumed, if sanction is given to withdraw the mechanical aids to continuation of life, that adequate and acceptable safeguards against careless and hasty diagnoses will be established. Again it must be pointed out that every situation is different: the age of the patient, the circumstances of those paying the bills, the possibility of new information which may be gained if the patient's life is prolonged, and so forth.

However, most ministers are reluctant to give an unqualified 'yes' to withdrawing the means of sustaining life, even in extreme cases. They are fearful that sanction might tend to cheapen life, that many individuals in a coma can be reached, and that they hear what is being said, though they give no outward response.

I personally believe these objections to euthanasia can be met and that letting nature take its course when the body is 'through' is both wise and kind.

Pastor Elmer S. Hjortland
Minneapolis, Minnesota

THERE HAS BEEN much discussion in religious groups as well as in medical organizations as to whether artificial respiration, blood transfusion and the like, should be applied in the case of a patient where there is every indication that death is inevitable. Some religious groups have agreed with this point of view, contending that a "patient has the right to die."

It seems to me that the principle motivating this attitude is the same as that of euthanasia, except in reverse. In euthanasia, death is brought about in a direct way. In the "patient has the right to die" theory, everything is withdrawn that might prolong life.

For instance, when an artificial respirator is keeping the patient alive, I would not accept the responsibility of advising the physician to turn it off, any more than I would counsel him to give the patient a drug that would result in his death.

The moral principle involved is the sanctity of life which we are commanded to preserve and not to destroy, regardless of circumstances.

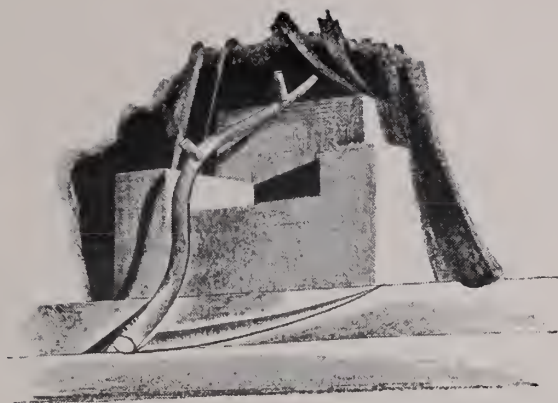
Rabbi Minda
Minneapolis, Minnesota

Real Happiness

I don't know what your destiny will be, but one thing I know: The only ones among you who will be really happy are those who have sought and found how to serve.

Albert Schweitzer

Fear clogs; Faith liberates.—Elbert Hubbard



In Memoriam

'Tis true; 'tis certain; man though dead retains Part of himself; the immortal mind remains.—Homer

AMES W. NASLUND, M.D.

Dr. Ames W. Naslund, 66, Edina radiologist, died August 13. Dr. Naslund, who graduated from the University of Minnesota Medical School, completed his residency in radiology at the University of Iowa. He was a faculty member of the University of Minnesota and former chief of radiology at St. Barnabas Hospital.

Also, he was a member of the Hennepin County Medical Society, American Medical Association, and the Minnesota State Medical Association.

Dr. Naslund is survived by his wife and two daughters.

WILLIAM CYRIL FERGUSON, M.D.

Dr. William C. Ferguson, 57, Walnut Grove physician, died September 5 of a heart attack. He was born in Wagon Mound, New Mexico, and obtained his medical education at the Nebraska University, College of Medicine.

He was a member of the Lyon-Lincoln Medical Society, American Medical Association, and the Minnesota State Medical Association.

He is survived by his wife.

JOHN H. GAMMELL, M.D.

Dr. John H. Gammell, 76, Minneapolis physician, died September 11. Born in Minneapolis and educated at the University of Minnesota, Dr. Gammell was a former chief-consulting oculist at the Minnesota Braille and Sightsaving School in Faribault.

He was a member of the Hennepin County Medical Society and American Medical Association and a Life Member of the Minnesota State Medical Association.

He is survived by his wife and four sons, one of whom is Dr. Gerald Gammell of Oshkosh, Wisconsin.

JAMES A. COSGRIFF, SR., M.D.

Dr. James A. Cosgriff, Sr., 75, president of the Asso-

ciation of American Physicians and Surgeons and Olivia physician, died September 5th at the Renville County Hospital following a long illness. Dr. Cosgriff, who had practiced medicine in Olivia for thirty-eight years, was a past president of the Minnesota Heart Association and the Minnesota Academy of General Practice.

He held many positions of note in his county and state medical societies, namely the Renville, Redwood County Medical Society of which he was president and the Minnesota State Medical Association. He was also a member of the American Medical Association.

He is survived by his wife and seven children, including Dr. J. A. Cosgriff, Jr. of Olivia.

ANDREW D. HOIDALE, M.D.

Dr. Andrew Hoidale, 90-year-old Tracy physician, died July 25. He was born in Tromsø, Norway, educated in Dawson and went to Tracy in 1904 where he practiced medicine until his retirement.

A graduate of the Minnesota School of Medicine, Dr. Hoidale held such city offices as mayor, councilman and health officer of Tracy and also served as a school board member. He was a member of the Lyon-Lincoln Medical Society and the American Medical Association and a Life and 50 Club Member of the Minnesota State Medical Association.

He is survived by one son and a daughter.

JOHN D. KEYES, M.D.

Dr. John D. Keyes, 64, Winona physician, died May 23. Born in Winona, Dr. Keyes received his education in Winona and practiced medicine there until his retirement. He received his degree of doctor of medicine from the University of Minnesota Medical School.

He was a member of the Winona County Medical Society, American Medical Association, and an Associate Member of the Minnesota State Medical Association.

He is survived by two children.

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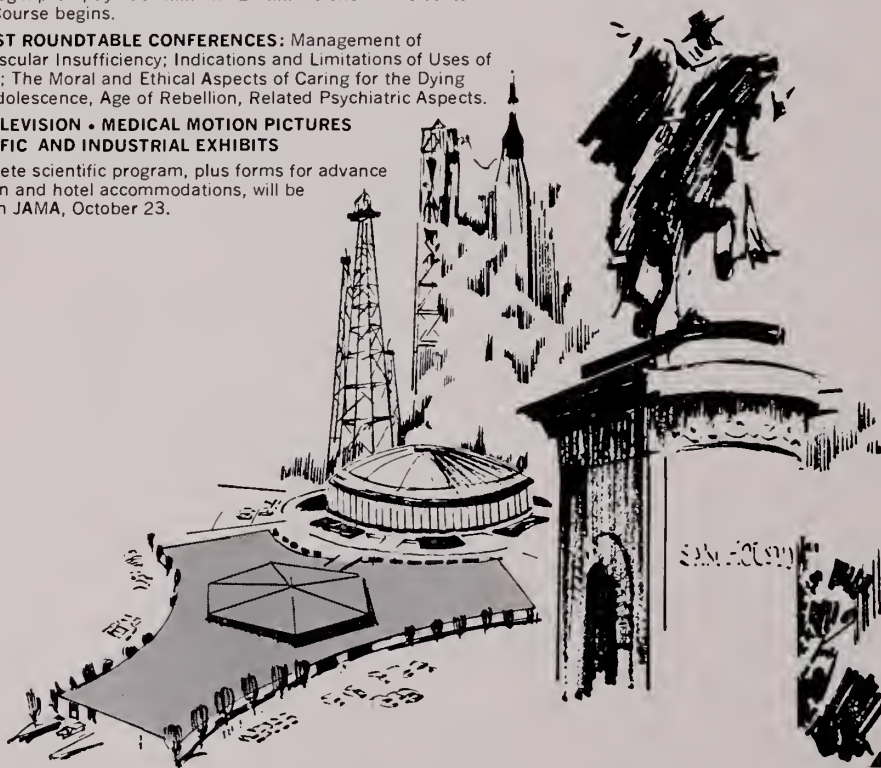
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Meetings and Announcements

Next to knowing when to seize an opportunity, the next important thing in life is to know when to forgo an advantage.—Disraeli

NOVEMBER

Minnesota Academy of Ophthalmology and Otolaryngology, No date set as yet.

Minnesota Psychiatric Society, Fall meeting, No date set as yet.

Zumbro Valley Medical Society, Regular Meeting, Plummer Hall, 8:00 P.M., November 1.

Southwestern Minnesota Medical Society, November 6, Ehlers Supper Club, 7:00 P.M.

Scott-Carver County Medical Society, November 7, Wagner Supper Club, Jordon, Minnesota, 7:30 P.M.

St. Louis County Medical Society, Executive Committee, St. Mary's Hospital, 6:00 P.M., Regular Meeting, St. Mary's Hospital, 8:00 P.M., November 9.

Blue Earth Valley Medical Society, November 15, Interlaken Golf Club, Fairmont, Minnesota, 7:00 P.M.

McLeod County Medical Society, November 16.

Twin City Urologic Society, November 17, Town and Country Club, St. Paul, 6:00 P.M.

Hennepin County Academy of General Practice Annual Invitational Banquet, Radisson Hotel, Minneapolis, 6:00 P.M. Social Hour, 7:00 P.M. Dinner, 8:00 P.M. Program, November 20.

Ramsey County Medical Society Regular Meeting, 1500 Lowry Medical Arts Building, St. Paul, 8:00 P.M., November 27.

Range Medical Society Regular Meeting, Hibbing, Minnesota, November 28, 7:00 P.M.

Postgraduate Course in Laryngology and Bronchoesophagology, November 6 to 17, Illinois Eye and Ear Infirmary, 1855 West Taylor Street, Chicago. Write: Department of Otolaryngology, University of Illinois, P.O. Box 6998, Chicago.

Clinical Reviews, Mayo Clinic, November 6, 7 and 8 and November 13, 14 and 15, Theater. Mayo Civic Auditorium, Rochester. Fee is \$10. Write: Mr. M. G. Brataas, Mayo Clinic, Rochester.

DECEMBER

Minnesota OB-GYN Society, St. Paul-Ramsey Hospital, 9:00 A.M., December 2.

Southwestern Minnesota Medical Society, December 4, Ehlers Supper Club, 7:00 P.M.

Scott-Carver County Medical Society, December 5, Wagner Supper Club, Jordon, Minnesota, 7:30 P.M.

St. Louis County Medical Society Executive Committee, St. Luke's Hospital, 6:00 P.M., December 14.

Annual Banquet, Kitchi Gammi Club, 7:30 P.M., December 16.

McLeod County Medical Society, December 21.

Minnesota Academy of Ophthalmology and Otolaryngology. No date set as yet.

American Academy for Cerebral Palsy, San Francisco-Hilton Hotel, San Francisco, Dec 10-14. Exec. Sec.: J. D. Russ, M.D., 1520 Louisiana Ave., New Orleans 70115.

American Academy of Dermatology, (E), Palmer House, Chicago, Dec. 2-7. Sec.-Treas.: Stanley E. Huff, M.D., 636 Church St., Evanston, Ill. 60201.

American Academy of Psychoanalysis (Mid-Winter) Hotel Summit, New York, Dec. Exec. Sec.: Mollie Carroll, 125 E. 65th St., New York 10021.

American Association for the Advancement of Science, New York, Dec. 26-31. Info: Dr. L. Taylor, 1515 Massachusetts Ave., N.W., Washington, D. C. 20005.

American Psychoanalytic Association, (E) (M) Waldorf Astoria Hotel, New York, Dec. 15-17. Exec. Sec.: Mrs. Helen Fischer, One E 57th St., New York 10022.

Delaware Academy of General Practice, (E), Delaware Academy of Medicine, Wilmington, Dec. 2. Sec.: Charles W. Wagner, 1925 Lovering Ave., Wilmington, Del. 19806.

Latin American Congress of Pathology (VI) and Pan American Meeting of International Academy of Pathology (I), (E), San Jeronimo Hilton, San Juan, PR, Dec. 10-17. Info: Raul A. Marcial-Rojas, M.D., Pres., School of Medicine, San Juan, PR 00905.

New York State Society of Anesthesiologists, New York Hilton Hotel, New York, Dec. 11-13. Exec. Sec.: Mrs. Eugenia C. Sinisi, 30 E. 42nd St., New York 10017.

Society of Cosmetic Chemists, Semi-annual, Americana Hotel, New York, Dec. 6. Info: Mrs. Eunice T. Miner, Adminis. Asst., 2 E. 63rd St., New York 10021.

Southern Surgical Association, The Homestead, Hot Springs, Va., Dec. 4-6. Exec. Sec.: Dr. George H. Yeager, 314 Medical Arts Building, Baltimore 21201.

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EASTERN WISCONSIN CLINIC in rapidly growing community of 50,000 desires board-eligible or certified physicians in obstetrics and gynecology, pediatrics, orthopedic surgery, urology and otolaryngology. Well-equipped clinic and excellent hospital facilities. Lake shore location offers ample recreational facilities. Attractive financial plan leading to early full partnership. Full expenses paid for applicants invited to interview. Call or write: F. L. Hildebrand, M.D., Riverside Clinic, Menasha, Wisconsin.

THREE MAN group in North West Wisconsin Resort, State Conservation and Retirement Area needs two more physicians adequately to serve their practice. Facilities offered are three-room physician suites, X-ray and lab under AMT technician, RN-only nursing personnel. New accredited thirty-two bed hospital and forty-six bed nursing home. Deer and duck hunting, fishing within five minutes of town. Internist most needed; generalists welcomed. Will meet any reasonable salary request. Partnership after one year. Write: MINNESOTA MEDICINE—365; 375 Jackson St., St. Paul 55101.

WANTED: GP to join clinic serving population area of 12,000. City has new hospital, new clinic building, two nursing homes, new Jr-Sr high school, new swimming pool, rich farming area in Red River Valley. Fishing and hunting nearby; metropolitan city close by. Salary open and partnership if interested. Write or call Warren Clinic, Warren, Minnesota 742-6231, area code 218.

WANTED: General practitioner, to join two G.P.'s well established in north central Minnesota community, 2200 pop., 65 miles from Twin Cities. Excellent office space with lab and X-ray, just opened new hospital, all facilities. Assistantship or partnership. Considerable surgery and obstetrics. Hunting, fishing, golf club. Great opening for interested G.P. WRITE MINNESOTA MEDICINE—381; 375 Jackson, St. Paul, 55101.

GENERAL PRACTITIONER wanted to join well-established practitioner. New clinic building—90 miles east of St. Paul—city of 14,000. Early partnership with full hospital facilities. Ideal location. L. W. Picotte, M.D.; Chippewa Falls, Wisconsin.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X-ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE—289; 375 Jackson, St. Paul, 55101.

WANTED: Locum Tenens for general practice for February, 1968. Salary open. Contact: Maurice Meller, M.D., Brainerd Clinic, Brainerd, Minnesota.

PHYSICIAN INTERESTED in internal medicine wanted for Medical Service. Starting salary \$12,873 to \$17,221, depending on qualifications. Liberal fringe benefits. Non-discrimination in employment. Contact Chief of Staff, Veterans Administration Hospital, Des Moines, Iowa 50308.

WANTED: Young, energetic General Practitioner to join one man clinic. Salary open. Contact: Maurice Meller, M.D., Brainerd Clinic, Brainerd, Minnesota.

WANTED: YOUNG PHYSICIAN for association leading to partnership with four well-established General Practitioners in fast-growing suburb of St. Paul. Excellent clinic facilities in nearly new, partnership owned, well equipped, medical center building. Contact: A. Eugene Muller, M.D., North St. Paul Medical Center, 2579 East 7th Avenue, North St. Paul, Minnesota 55109.

SAN FRANCISCO AREA: G.P.'s and/or Internists to associate with group in fascinating Bay Area; Salary open. Partnership and locum tenens available. A. J. Franzi, M.D., 3620 Army St., San Francisco, Calif. 94110.

GENERAL PRACTITIONER OR INTERNIST needed in six man group in Northeastern Minnesota. 38 bed accredited hospital next door to modern clinic, rotating call schedule, over 4 wks. vacation per year, study and sick leave, group paid disability and retirement plans, and full partnership in 6 months. Starting guarantee \$18,000 to \$22,000 with increases to \$26,000 to \$28,000 over 4 years. Ideal opportunity for man desiring association with active group in small community offering good income plus ample time off. Contact Harold B. Leppink, M.D., Community Clinic, Two Harbors, Minnesota. Phone Area 218 834-2171.

MORGAN, MINNESOTA, Wants a General Practitioner. Opportunity to take over a well established practice. Physician recently retired after practicing here for 33 years. Progressive community in the best rural area of Southern Minnesota. New medical clinic building just completed. Call or write M. L. Kuhn, Morgan, Minnesota. Tel. Morgan #73 or #99.

WANTED: INTERNIST to enlarge busy internal medicine department in highly successful nine man specialty group. All are board certified. Well equipped lab and x-ray—new 120-bed hospital. Pleasant community of 15,000 plus on Mississippi River. Good recreational facilities, not far from Twin Cities. Salary one year then partnership. Write: George E. Jackish, M.D.—Interstate Clinic, Red Wing, Minnesota or call 507 388-3503.

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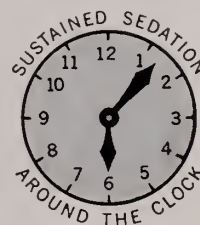
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WANTED: G.P. to take over practice located in East Side of St. Paul, including equipment and lease, all available with good financing. Retiring G.P. will practice to acquaint buyer with patients. Write: MINNESOTA MEDICINE—386, 375 Jackson, St. Paul 55101.

GENERAL PRACTICE associate wanted for young three man group in populous growing area located 30 minutes south of the Twin Cities. Spacious three year old clinic with new accredited hospital and nursing home in same town. Salary and terms open. Contact River's Edge Medical Clinic, Farmington, Minnesota. Telephone 463-7181.

PHYSICIAN WANTED: G.P. with additional surgical and OB experience—desired to associate with two G.P.'s with similar experience in large, well established practice in Central Minnesota. Hospital accredited, 300 bed, open staff, complete services. Salary leading to partnership. Adequate housing in area. Send background information, professional and personal to: MINNESOTA MEDICINE-283, 375 Jackson, St. Paul 55101.

GENERAL PRACTITIONER WANTED: To associate with physician-surgeon in Owatonna, a Southern Minnesota community, 25,000 population. Clinic building three years old; with five large treatment rooms; lab; x-ray; central supply; two doctors' offices; pharmacy; and business offices. Located next door to 85-bed city hospital. Good opportunity for partnership. Contact: O. W. Roberts, M.D., 920 So. Cedar St., Owatonna, Minnesota Phone 451-4630.

INTERNIST ASSOCIATE wanted in Pacific Northwest city of 170,000. Low humidity, no ragweed, fabulous recreational area. Expanding practice to accommodate second internist. New multi-specialty building adjacent new hospital in residential area. All hospitals open staff. Further details by correspondence only. Give curriculum vitae first letter. Write: MINNESOTA MEDICINE-382, 375 Jackson, St. Paul 55101.

MEDICAL GAL FRIDAY: R.N. desires position in Drs. office in St. Paul loop area 5 days a week. No Sat. Former surg. nurse; 5 yrs. experience in Drs. clinics; 11 mos. experience processing Military Medicare claims, lite typing, no shorthand or dictaphone exper. Good references. Salary needed \$450-\$500. Phone 755-3951 after 6 P.M.

PSYCHIATRIC RESIDENCIES: Accepting applications for January and July 1968. Balance didactic-clinical program providing extensive, varied experience with both inpatient and outpatient adults and children. Fully approved three year training. Three year plan: \$8,978, \$9,417, \$10,210. Five year career plan: \$10,231, \$11,797, \$13,739, \$17,497, \$18,458. Located in Michigan's serene, scenic water wonderland. Contact: Dr. Paul E. Kauffman, Director of Training, Traverse City State Hospital, Traverse City, Michigan 49684. An equal opportunity employer.

GENERALIST AS MEMBER of Medical Staff of progressive State Hospital in Michigan's Vacationland. Hospital has 3-year accreditation, JCAH and 3-year residency accreditation by A.P.A. Salary \$16,000 to \$19,800. Excellent fringe benefits. Civil Service Security when qualified. Apply L. B. Young, M.D. Director of Medical Services, Traverse City State Hospital, Traverse City, Michigan 49684.

WANTED—GENERAL PRACTITIONER to continue active solo practice of Doctor, who is leaving to join Metropolitan group practice. Two year old, medicare approved, twenty-five bed hospital with complete laboratory and X-ray facilities. Well equipped clinic for one or two doctors available without initial investment. Large consolidated schools, fine churches in prosperous dairy farming area. Hunting, fishing, golfing only minutes away. If you want to enjoy a profitable and satisfying career in a healthy environment for you and your family, you may find this a wonderful opportunity. Write, MINNESOTA MEDICINE-388, 375 Jackson, St. Paul 55101.

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Clinical Reviews

A program of lectures and discussions on problems of general interest in medicine and surgery. Mayo Clinic and Mayo Foundation, Rochester.

Identical sessions are offered on November 6, 7 and 8 and November 13, 14 and 15, 1967, Theater—Mayo Clinic Auditorium, Rochester, Minnesota.

This program is acceptable for credit by the American Academy of General Practice and the College of General Practice of Canada.

The registration fee for this program is \$10.

Those wishing to attend should communicate with Mr. M. G. Brataas, Mayo Clinic, Rochester, indicating which session they would prefer to attend.



Physician's Diary

The general principles of urbanity, politeness, or civility, have been the same in all nations; but the mode in which they are dressed is continually varying. The general idea of showing respect is by making yourself less; but the manner, whether by bowing the body, kneeling, prostration, pulling off the upper part of our dress, or taking away the lower, is a matter of custom.—Sir J. Reynolds

New Location:

Dr. Charles F. Turbak is now associated with Doctors Patrick Meekin, Thomas Meany and Joseph Stenzel in Columbia Heights. . . . Dr. Roger Slanga has opened offices for the practice of medicine in association with Dr. William A. Autrey in St. Cloud. . . . Dr. Milton Sadd has opened up offices in Willmar where he will specialize in dermatology. . . . Dr. Barlow Smith has opened offices for the practice of psychiatry in the Southdale Medical Building in Edina. . . . Dr. Lawrence R. Boies has accepted a position as President of the Deafness Research Foundation in New York City.

* * *

Dr. R. W. Bergstrom, Jr., M.D., has joined Dr. Leland Christenson in his medical practice in Maple Plain. . . . Dr. Dudley Wilkinson is now associated with the Peterson Clinic in Mora. . . . Dr. Hildegard K. Graber of Newport has been appointed assistant medical director of the Hastings State Hospital. . . . Dr. Robert G. Hankerson has left Minnesota Lake to take up duties at the dispensary at Mankato State College in Mankato.

* * *

Doctors Donald A. Wolochow, Raymond A. Allen, William F. Taylor, Mark S. Schwartz, Robert V. Pierre, Walter R. Lysak, Gordon L. Moore, II, Malcolm I. Lindsay, Jr., Frank J. Leary, Leo J. Davis, Jr. and Claude D. Arnaud have been appointed to the staff of the Mayo Clinic in Rochester.

* * *

Dr. William ReMine, Mayo Clinic surgeon, was named president-elect of the Priestley Society at their annual meeting in May, and Dr. Waltman Walters, emeritus senior surgeon of the Mayo Clinic, has been elected as honorary member of the section of surgery of the German Society for Clinical Medicine of East Germany.

* * *

Dr. Kenneth Huizenga, a Mayo Clinic staff member, has been appointed to the national YMCA's International Committee.

A new book "Ultrastructure of Normal and Abnormal Skin" was published by Lea and Febiger Company of Philadelphia. Dr. A. S. Zelickson of Minneapolis is the author. The book has 528 pages.

* * *

Dr. Khalil G. Wakim, a member of the Section of Physiology of the Mayo Clinic, recently was invested with Knighthood in the Order of the Cedar of the Republic of Lebanon at Beirut. He also received a gold medal and a distinguished alumnus award from the American University of Beirut.

* * *

Dr. Joe M. Neal has retired from the Veterans Administration Service in Minneapolis after forty-seven years. No special plans have been made by Dr. Neal for his retirement.

* * *

Dr. Jurgen J. Moller, a resident in anesthesiology, University of Minnesota Medical School, is the latest Minnesota physician to participate in the Volunteer Physicians for Viet Nam Program. He departed for Viet Nam on September 22.

* * *

Dr. Dale J. Eichelberger, Willmar, has been elected to active membership in the American Academy of General Practice.

* * *

Dr. Henry Buchwald, assistant professor of surgery at the University of Minnesota, has been awarded the Samuel D. Gross Prize in Surgery by the Philadelphia Academy of Surgery.

Dr. Buchwald will go to Philadelphia this fall to receive his \$1,500 prize money and present his award-winning thesis: "A Laboratory and Clinical Study of Cholesterol Metabolism and Atherosclerosis as Influenced by Partial Small Intestinal Exclusion."

He is the third University of Minnesota surgeon to receive the Gross Prize for Surgery. Dr. Owen Wangenstein received it in 1935 and Dr. George Moore in 1950. The prize was first awarded in 1895 and has been presented to some 15 surgeons who have made original contributions in their fields.

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Minnesota Medicine at a Glance

Aortic Stenosis and Unexplained Gastrointestinal Bleeding—
Nordstrom and Myhre

Page 1623

The authors describe a very interesting patient with aortic stenosis who has had multiple hospital admissions for gastrointestinal bleeding, the site and cause of which could not be established. They point out that there have been a number of reports in the literature indicating an apparent association between aortic stenosis and recurrent gastrointestinal bleeding of unknown etiology. The incidence of aortic stenosis in patients with unexplained gastrointestinal bleeding has been reported to be five times greater than in the rest of the population.

The Lifegame—Buckley

Page 1631

The events of life are many and various. Yet they tend to trigger some rather consistent physiologic responses, which are an important part of the "personal life style" of each individual. This paper explores some of the neurophysiologic "groundrules" for experiencing life, and then acting with it, and on it, and in it.

Traumatic Brain Syndrome Undergoing Remission—Luckey

Page 1637

Any disease or illness may be accompanied by psychological and social problems which excessively complicate or even supersede in complexity a patient's organic illness. Physicians must be prepared to foresee and manage all aspects of a patient's illness with the ultimate goal of returning that patient to society as a productive member.

This presentation aptly describes a case of traumatic encephalopathy in which eventual improvement of the patient's organic illness was accompanied by personal and social difficulties that complicated his road to recovery. Several suggestions are made by the author for dealing with these problems.

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DECEMBER, 1967

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References: 1. Batterman, R. C., and Grossman, A. J.: *Fed. Proc.* 14:316, 1955. 2. Goodman, L. S., and Gilman, A., ed.: *The Pharmacological Basis of Therapeutics*, ed. 3, New York, The Macmillan Company, 1965, p. 331. 3. Roth, J. L. A., et al.: *Gastroenterology* 44:146, 1963. 4. Conney, A. H., and Burns, J. J.: *J. Pharmacol. Exp. Ther.* 123:340, 1960. 5. Settler, E.: *Clin. Med.* 6:1373, 1959. 6. Berman, H. H., et al.: *Dis. Nerv. Syst.* 25:430, 1964. 7. Darienzo, C.: *Ibid.*, 27:189, 1966.

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President's Letter

FOR MANY REASONS I want to make my last President's Letter one to fit the season. Hence I choose to write on the general topic of "Medicine and Religion." I have never been, nor ever will be, one who wears his religion on his sleeve, as it were. However, I am perfectly willing to stand up and be counted when the occasion arises that this type of action is appropriate. Such is the case now.

I propose to tell you about a very personal experience which is, as I prefer to think, a story to further document evidence that there is some Power greater than any we know of on this earth, which guides our destinies. Obviously the first necessary ingredient is Faith. The skeptic, agnostic, or atheist lacks this particular quality, and such is his privilege. But I feel genuinely sorry for anyone who lacks this thing called Faith, as he is missing something which can, in a time of personal tragedy or loss, provide a greater measure of solace than anything else I know of.

As you may have guessed, these letters are written about three months in advance, and it so happens that I have just sustained the loss of both my 93-year-old mother and my 51-year-old brother within less than eight hours during one memorable night in August, 1967. My brother was one of those unfortunates who was born mentally retarded, a victim of mongolism. For years Mother had hoped and prayed that he could precede her in death, so that her devoted and dedicated service on his behalf would terminate before she died.

It happened exactly that way!!! Warren died at 9:30 P.M. on the night of August 28th,

and Mother followed at 5 A.M. on August 29th. I am sure she was aware that he was going to go soon, as she knew of his critical illness before she herself underwent her own final stroke and pneumonia. But it seems inconceivable to me that these two deaths could have occurred by pure chance as close together as they did and also in the sequence in which they did. As I am no mathematician, I cannot quote the odds against its being a coincidence; but those odds must be fantastically high. Yet it did happen.

Such an occurrence should make even the most skeptical of unbelievers pause and reconsider. *Ipse res loquitur!!!* I must freely admit that my own Faith got a tremendous boost when this happened. My mother's own unflagging Faith had been vindicated and substantiated! Had she known about it, and I'm inclined to think that she did, she would not have been at all surprised. Even to those of us who profess ourselves Christians, it was an astounding event!!

We as physicians are in an extremely advantageous position, if we are willing to take the opportunities which present themselves, to quietly and unostentatiously strengthen the Faith of our patients, their families and friends in their moments of doubt and sorrow. We have all encountered deaths among our patients and have been called upon to comfort their families. Can you conceive of a physician-atheist giving any genuine solace to the bereaved? A statement came out of World War II: "There are no atheists in foxholes!!"

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Radical Pancreatoduodenectomy

BERNARD F. L'ESPERANCE, M.D.
Two Harbors, Minnesota

APERUSAL OF the medical literature during the past decade gives credence to the fact that radical pancreatoduodenectomy has under great duress finally achieved its just recognition as a treatment of some merit for cancer in the region of the terminal common bile duct and head of the pancreas. That this recognition has been slow in developing is understandable when one reviews the natural history of the operation.

Prior to 1935, diseases of the pancreas were regarded as exercises in diagnostic acumen and surgically abandoned because of the technical difficulties involved and the grave consequences resulting from surgical assault on this organ. Whipple,¹ in 1935, courageously led the avant-garde in the surgical approach to pancreatic disease. His work was greeted with great enthusiasm and vigor; however, optimism was soon replaced by pessimism induced by the subsequent morbidity and mortality following these operations, and, just as important, because of the low permanent salvage rates which ensued. It is unfortunately true that a significant number of the medical profession today still look on the operation with disdain and pessimism. In the light of recent reports this attitude becomes untenable.

Circumstances being favorable, pancreatoduodenectomy becomes the procedure of choice in cases of cancer in the region of the terminal common bile duct and the head of the pancreas. Pessimism should be tempered by optimism; patients presenting with resectable lesions must be given every opportunity for cure—a cure realized only by surgery. Anything less predetermines the patient's fate; undoubtedly many palliative and routine by-pass procedures have deprived a significant number of patients of the opportunity for cure and/or pain-free palliation.

Pancreatoduodenectomy is a formidable undertaking; perhaps this alone deters some from attempting it. With the availability of major medical centers today, if a resectable

lesion is encountered at the operating table and the surgeon is unequipped to perform the operation, a by-pass procedure may or may not be performed and the patient referred for definitive handling of the problem. In most instances "T" tube decompression of the biliary system can be carried out and the patient transferred.

Encouraging survival rates and decreasing mortality rates are being reported by those experienced in this field. Mongé, Judd, and Gage,² reporting from the Mayo Clinic on a twenty-two-year experience (1941-1962) with radical pancreatoduodenectomy, reviewed 239 cases with an overall mortality rate of 19.2%. The five-year survival rate of those operated prior to January, 1959, and broken down as to site of origin of the disease, totaling 134 cases; and a similar series reported by Warren³ et al. giving statistical information on 211 cases of periampullary carcinoma in which pancreatoduodenectomy had been performed with a mortality rate of 11.4% are compared in Table 1. Concerning the carcinoma of the ampulla of Vater Warren stated that when the initial definitive procedure was performed at the Lahey Clinic, 52% of patients survived five years or more. Certainly such reports shed a more favorable light on judiciously applied pancreatoduodenectomy.

Procedure

In each instance the exposure through long upper right paramedian incision has been found to be quite adequate. The procedures were performed under general anesthesia, using nitrous oxide, oxygen, and ether administered through an indwelling endotracheal tube. Appropriate preoperative preparations using whole blood, and parenteral vitamin K, when indicated, were carried out. The procedure we utilized was similar to Waugh's⁴ modification

of the Whipple operation.

Operability is determined by the degree of involvement or lack of involvement of the superior mesenteric vessels, the portal vein, and other regional retroperitoneal structures. This may be determined before committing oneself to the operation by freeing the hepatic flexure of the colon, dividing the right gastocolic omentum, and incising the peritoneum at the inferior margin of the head and neck of the pancreas. The duodenum and head of the pancreas are mobilized by incising the parietal peritoneum lateral to these structures; the right gastric and gastroduodenal arteries are divided. After these primary maneuvers are completed, one is able to pass a finger posterior to the pancreas and duodenum superoinferiorly along the anterior surface of the portal vein and superior mesenteric vessels to emerge at the inferior margin of the pancreas. The decision to initiate or abandon the procedure is made at this juncture. If abandoned, then a biliary by-pass is done; and in some cases, depending on the degree of duodenal obstruction, a gastrojejunostomy is carried out. If regional involvement and liver metastases are present and the lesion is still resectable, consideration can be given to performing a palliative resection. Some authors have gone so far as to resect a portion of the superior mesenteric vessels and portal vein. However, it would seem that the added risk attendant on this, coupled with the questionable immediate or long-range benefit, would hardly justify its performance.

Obesity, which adds to the technical difficulties of all surgical procedures, certainly compounds the problems here. In such cases, it is probably best to forego resection and simply plan on relieving the biliary and intestinal obstruction.

After the specimen, including stomach, head and neck of pancreas, terminal common bile

TABLE I

	Mongé-Judd ²	Warren ³
Total Cases	239	211
Over-all Mortality	19.2	26.9
Site of Origin	Five-Year Survival	Five-Year Survival
Carcinoma of Pancreas	18.2%	6.4% (Head of-)
Carcinoma of Duodenum	38.5	40.
Carcinoma of Common Bile Duct	11.1	36.4 (intrapancreatic-)
Carcinoma Papilla Vater	39.1	31.3

duct, and duodenum, is removed en masse, the jejunum is brought through the defect created when the ligament of Treitz was divided and made to occupy that position formerly held by the duodenum. An essential feature at this point is to ensure adequate blood supply to the replacing jejunum. After the body of the pancreas is adequately mobilized, an end-to-end pancreatojejunostomy is performed, inverting the end of the pancreas into the jejunum, with two rows of interrupted silk and with no attempt at mucosa-to-mucosa apposition. The end-to-side choledochojejunostomy is carried out distally at a comfortable level and an anterior gastrojejunostomy with Hofmeister modification is done. Drainage of the operative area is routine. Postoperatively, nasogastric drainage is maintained until active peristalsis appears and the patient is passing flatus per rectum. Attention to fluid and electrolyte replacement is essential for a successful outcome.

Case Reports

Case 1

A 73-year-old female was seen in November 1959 with a twelve-month history of epigastric and back pain, aggravated by eating and associated with anorexia and a twenty-pound weight loss.

She had undergone a cholecystectomy twenty years previously for cholelithiasis.

Physical Findings

Physical examination revealed an elderly, thin, pale female weighing 130 pounds. The pertinent finding was a questionable tender mass in the right epigastrium. All laboratory studies were negative except for an elevated sedimentation rate of 75 mm. per hour. Intravenous cholangiogram revealed a dilated common bile duct with evidence of an obstructing nonopaque stone in the distal portion.

Surgical Findings

Exploratory laparotomy uncovered a firm orange-sized mass in the region of the head of the pancreas. The common bile duct was dilated two to three times its normal size. Microscopic study of the frozen biopsy section indicated a mucinous adenocarcinoma. The liver was free of metastases; there appeared to be no peritoneal seeding, nor was there any immediate evidence of direct involvement of adjacent vital structures. The lesion appeared resectable and the radical pancreatoduodenectomy was carried out.

During and immediately following the procedure the patient received 1500 cc. of blood.

Postoperative Course

Postoperatively, bile drainage through the drain site was profuse for five or six days but subsided sponta-

neously. Recovery was otherwise uneventful and the patient was discharged on the sixteenth postoperative day. Study of the surgical specimen disclosed a mucinous $7 \times 5\frac{1}{2} \times 5\frac{1}{2}$ -cm. adenocarcinoma of the pancreas, probably originating from the pancreatic duct. There was marked atrophy with almost complete disappearance of the excretory portion of the pancreas but no evidence of regional lymph node metastases, and there was secondary ulceration of the duodenum with tumor tissue protruding into the lumen. The patient has been followed regularly since her surgery. Shortly postoperatively she developed a tendency toward steatorrhea which has been controlled with oral pancreatic extract; and periodic tests for diabetes have failed to show this development. She required re-admission to our hospital in June 1965 because of small bowel obstruction due to a single adhesive band which required surgical division. At this time there was no evidence of intraperitoneal recurrence of the tumor. She is still clinically free of cancer. (This case represents an eight-year survival following pancreatoduodenectomy for a carcinoma of the head of the pancreas.)

Case 2

A 72-year-old male was seen February 17, 1961, with a history of painless jaundice of three weeks' duration. Physical examination revealed a deep icteric tinge to the skin and conjunctiva and an enlarged liver three finger breadths below the costal margin. Laboratory studies were compatible with the obstructive jaundice; liver function tests were normal. X-ray investigations were also normal.

Surgical Findings

Exploration was performed March 3, 1961, after several days of preoperative preparation and revealed a large greenish liver and distended gallbladder. On palpating the pancreas there was a small 2×3 -cm., ill-defined, indurated nodule located in the region of the ampulla of Vater. Choledochostomy was performed and exploration of the common bile duct was negative. A duodenostomy was then carried out and this, too, was without pathological finding. After the head of the pancreas and duodenum were mobilized by incising the peritoneum laterally, numerous biopsies taken in the region of the common bile duct and head of the pancreas were negative. Because of the history, localized nature of the lesion, and lack of obvious distant or local spread, it was decided to perform the Whipple procedure. The cystic duct was long and entered the bile duct close to the proposed site of anastomosis; so a cholecystectomy was also performed. The procedure was carried out as in the previous case. During and immediately following the operation the patient received four units of blood. Postoperatively he developed a pancreatic fistula which closed spontaneously in three weeks.

Postoperative Course

The jaundice and pruritus gradually disappeared, his general condition improved, and he was discharged six weeks postoperatively. Study of the surgical specimen revealed a $3 \times 2 \times 1\frac{1}{2}$ -cm., early mucinous adenocarcinoma of the pancreas (ductal type) with one regional lymph node involved by the tumor. There was also

constriction of the common bile duct by scar tissue and early neoplastic infiltration. He was re-admitted to the hospital in January 1963 with recurrence of his carcinoma and expired January 13. Autopsy confirmed the recurrence, and a stomal ulcer was noted. (This case represents a palliation of approximately 19 months, during which time the patient was relatively free of pain and there was no recurrence of the jaundice.)

Case 3

A 59-year-old female was admitted to the hospital July 20, 1962, with a four-week history of pain and jaundice.

Physical examination revealed severe jaundice with the liver palpable two finger breadths below the costal margin, smooth and nontender. Laboratory studies showed hemoglobin of 10.3 grams or 71%; a white blood count of 8,600; a prothrombin time of 14.5 seconds as compared with control of 12 seconds; a thymol turbidity of 5.2 units; a serum albumin of 3.4 grams; a serum globulin of 2.8 grams; a total protein of 6.2 grams. Pre-operative preparation consisted of blood transfusions to restore the circulating blood volume, administration of parenteral vitamin K, multivitamins, and a high carbohydrate-high protein-low fat diet.

Surgical Findings

Exploration on September 2, 1962, revealed a tremendously dilated common bile duct. The gallbladder had been removed previously. Choledochotomy was carried out and one small stone removed. During the course of dilating the sphincter of Oddi, a small firm mass was palpated in the region of the ampulla of Vater. Transduodenal investigation revealed what appeared to be a carcinoma of the ampulla which was confirmed by biopsy. The Whipple procedure was performed, during which two units of blood were administered. The patient's postoperative course was uneventful and she was discharged home on the twenty-first postoperative day. The pathologist's report on the specimen was adenocarcinoma of the papilla of Vater with one regional lymph node involved.

Postoperative Course

She was seen regularly after surgery and was re-admitted to the hospital in November 1964 with severe back pain and jaundice. Exploration revealed extensive recurrence of carcinoma in the region of the porta hepatis and both lobes of the liver. The patient remained hospitalized and experienced a gradual decline until her demise January 1965. (This patient experienced a two-year palliation.)

Case 4

A 63-year-old female was admitted to the hospital May 14, 1965, to undergo surgery for chronic cholecystitis and cholelithiasis.

Operative Findings

Celiotomy was performed on May 15, 1965, at which time examination of the entire abdomen was negative except for the gallbladder which contained stones and the common bile duct which appeared enlarged. Cholecys-

tectomy was performed. An operating room cholangiogram showed a filling defect in the region of the ampulla of Vater, consistent with a stone. Choledochostomy was undertaken and the duct system scooped and generously irrigated; however, no stones were recovered. The sphincter of Oddi dilated readily and freely admitted a #5 mm. Bakes dilator. A duodenostomy was then carried out and a peculiar sessile type elevation encountered, overlying the papilla of Vater and extending a few mm. on to the duodenal mucosa. Frozen section study revealed a low-grade adenocarcinoma arising from the duodenal mucosa or from the papilla. Radical pancreatoduodenectomy was performed, during which the patient received three units of blood. Convalescence was entirely without incident and she was discharged on the fourteenth postoperative day. Microscopic examination of the resected specimen revealed the presence of a low-grade papillary adenocarcinoma of the papilla of Vater; all lymph nodes were negative.

Since the operation the patient has been followed at regular intervals and has done well with the exception of some difficulty in maintaining her weight.

Case 5

Presently there is in our hospital a 62-year-old male convalescing from surgery performed ten days ago. He presented with obstructive jaundice. Exploration October 31, 1967, revealed a greatly distended gallbladder and common bile duct. A firm ill-defined mass was palpated in the head of the pancreas adjacent to the common duct. Biopsy of an enlarged lymph node in this area was negative. Exploration of the extrahepatic duct system was negative. The pancreas was not biopsied. The decision was made to proceed with pancreatoduodenectomy because of the history and operative findings.

The pathologist reported a well differentiated 2 x 1½ cm. adenocarcinoma of the pancreas pressing on but not invading the common bile duct. All lymph nodes were negative. Tumor was present in nerve trunks and perineural lymphatics.

Comments

The role of radical pancreatoduodenectomy in the treatment of cancer is established. Reasonable morbidity and mortality and acceptable survival rates warrant an increasing judicious application of the procedure for cancer encountered in the region of the terminal common bile duct. Cure can result only if the malignancy is removed, and the only adequate operation that ensures this is the Whipple procedure. What is also not greatly appreciated is the fact that in many instances where cure does not result, reasonable palliation can be effected. The operation is difficult and time-consuming, but this should not be reason to ignore it.

The Role of Biopsy

From our brief experience and the experience of others, it can be reasonably stated that biopsy and frozen section analysis play a somewhat limited role in the differential diagnosis of pancreatic disease. In a large percentage of inoperable carcinomas, microscopic confirmation is possible. However, in the more important instances of operable lesions suitable for pancreatoduodenal resection, definitive diagnosis through biopsy is not always possible or absolutely necessary. Biopsy of the pancreas is by no means an innocuous procedure, especially when one tries to secure an adequate sample for frozen section. There is real risk of severe hemorrhage inherent in biopsy; cases of fulminating pancreatitis have been recorded following attempts to establish diagnosis through this medium. Although a positive diagnosis is reassuring, much time should not be spent in obtaining it. Nothing is more frustrating and unrewarding than spending a great deal of time attempting to establish a diagnosis through biopsy and ending up failing to do so. Biopsy of a regional lymph node may shed some light as to diagnosis when there is metastatic involvement. In some instances clinical judgment alone must determine. If a resectable lesion is discovered and the findings complement the historical data, it is best to proceed with the operation.

Stomal Ulcers

At autopsy Case 2 presented a stomal ulcer, a complication which has been noted by others. In our first two procedures we divided the stomach at the junction of its middle and lower third. However, after noting the development of a stomal ulcer in Case 2, we performed a two-thirds resection of the stomach in Cases 3, 4, and 5 and will continue to resect the greater amount in the future. Some have mentioned that perhaps a vagotomy and a more limited resection would be the preferred method of handling the stomach; however, appreciating the possible effect vagotomy may have on bowel function and the fact that a good percentage of patients following the Whipple procedure do have some bowel difficulties, it would perhaps be best not to perform a vagotomy. In addition, should a fistula develop, the way is open for a possible mediastinitis.

Cholangiogram

Case 4 demonstrates the wisdom of performing cholangiograms at the operating table. Operative cholangiograms have reached the stage where they have become an integral part of biliary tract surgery. Failure to perform these routinely when indications are present denotes a degree of incompleteness in the performance of the procedure. No great amount of special equipment is needed nor is much time expended in performing it. Interpretation of the cholangiograms increases with experience, and ductal pathology otherwise missed will be discovered—a consequence rewarding to both patient and surgeon.

Other Coincident Cases

During the period these procedures were being performed three palliative by-pass operations were carried out, two on patients aged 78 and 73, with inoperable carcinoma of the head of the pancreas and one on a 58-year-old poor-risk, obese, post-stroke patient with carcinoma of the terminal common bile duct. The three survived ten days, two months, and eleven months respectively. A radical pancreatoduodenectomy and a right hemicolectomy were successfully performed on a 75-year-old patient for an adenocarcinoma of the hepatic flexure which had extended to and perforated into the second portion of the duodenum.

Pancreatoduodenectomy is a formidable undertaking and should be undertaken only by those properly qualified. Not only is technical competence essential, but familiarity in the handling of postoperative problems is equally important, particularly in those patients with fluid and electrolyte imbalance. Constant diligent supervision is mandatory and is the sole responsibility of the operating surgeon, aided by round-the-clock special nursing. Our hospital though small is well equipped, possessing a laboratory where all chemical and electrolyte determinations are possible and a well organized blood bank provides ready access for replacement. Competent anesthesia, without which surgery of this magnitude would be impossible, is capably administered by resident physicians with special training in this field.

We have been impressed with the manner in which patients, regardless of their age, have

been able to tolerate a procedure of such magnitude. When proper detail is given to preoperative preparation, anesthesia, surgical technique, and postoperative care, mortality and morbidity can be kept at a reasonable level.

Summary

Five cases of successful radical pancreatoduodenectomy, three for carcinoma of the head of the pancreas, one free of tumor for eight years following initial treatment, one experiencing a nineteen-month palliation, and one experiencing an uncomplicated convales-

cense in hospital at this time; two for carcinoma of the papilla of Vater, one still living without evidence of disease twenty-eight months after surgery, and one succumbing two years after treatment, illustrate the value of this procedure under variable circumstances.

Three instances of palliative by-pass operation, with respective survivals of ten days, two months, and eleven months and a case of radical pancreatoduodenectomy and right hemicolectomy for cancer of the hepatic flexure of the colon were coincidental procedures for similar symptoms.

References

1. Whipple, A. O., Parsons, W. B., and Mullins, C. R.: Treatment of Cancer of Ampulla of Vater. *Ann Surg* 102:763, 1935.
2. Monge, J. J., Judd, E. S., and Gage, R. P.: Radical Pancreatoduodenectomy: A Twenty-two Year Experience with the Complications, Mortality Rate, and Survival Rate. *Ann Surg* 160:711, 1964.
3. Waren, K. W., McDonald, W. M., Veidenheimer, M. C.: Trends in Pancreatic Surgery. *S Clin North America* 44:743, 1964.
4. Waugh, J. M. and Giberson, R. C.: Radical Resection of the Head of the Pancreas and of the Duodenum for Malignant Lesions: Some Factors in Operative Technique and Preoperative and Postoperative Care, With an Analysis of 85 Cases. *S Clin North America*, pp. 965. August, 1967.

It's the Law

Attorney Awarded \$500 Fee for Recovering \$45.50 Fee for Physician

Three physicians, who treated the injuries sustained by an employee while at work, submitted fees for \$160, \$60, and \$55.50. The first two claims were rejected because of technical reporting requirements. The third bill received payment of \$45.50. The attorney, who prosecuted the claims of the physicians, requested a fee of \$1225 for his services. In support of his request, he submitted an itemized, sworn statement showing that he had spent about 35 hours in preparing, briefing, and arguing the case. Since the attorney was at least partially successful, he was entitled, under the statute, to a fair and reasonable fee. A fee of \$500 was awarded to the attorney for that part of his work allocable to the portion of the proceedings in which some success was achieved. The court ruled that despite the disproportion between the fee and the amount recovered, the fee was not unfair.

Case Reference—*Palumbo v. United States Rubber Company*, 229 A. 2d 620 (R.I., May 17, 1967).

Hayem-Widal Syndrome

Long known as Hayem-Widal syndrome this hematologic disorder is now usually termed "acquired hemolytic anemia." Its clinical characteristics consist of decreased red blood count, spherocytosis, icterus, and splenomegaly. Increased osmotic fragility of red corpuscles to hypotonic salt solution, a positive direct Coombs' test, and the presence of both warm and cold auto-antibodies are valuable supporting diagnostic criteria. Abnormal hemolysins are regarded as the cause. The anemia may be severe and the illness profound. Splenectomy is indicated and usually results in a cure.

Durham, Robert H.—*Encyclopedia of Medical Syndromes*
Hoebner Medical Division, Harper and Row, New York

Caplan's Syndrome*

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IN 1953, CAPLAN¹ called attention to an association of nodular fibrosis of the lungs with rheumatoid arthritis in coal miners. Since Caplan's original description, the syndrome has been reported²⁻⁴ to occur in workers exposed to other types of dust. The clinical complex is of interest because the soft-coal workers' exposure to silica was minimal. It may be not only a syndrome but also an interesting corollary of the interaction between silicosis and hypersensitized tissues. Pulmonary involvement can occur in cases of rheumatoid arthritis without exposure to irritating dust, and it can result in pleural thickening, pleural effusion with a low glucose content, and diffuse or focal interstitial fibrosis. However, the rheumatoid lung characteristically does not show the nodular fibrosis that is seen in Caplan's syndrome.

Observations

Sixteen patients with pneumoconiosis†, consisting of nodular fibrosis of the lungs, associated with rheumatoid arthritis were seen at the Mayo Clinic in the 10 years 1955 through 1964. Twelve were foundry workers; the remainder included a coal miner, a granite polisher, a textile-mill worker, and a rubber-factory worker (this patient had experienced prolonged exposure to rubber dust). Duration of exposure varied from two to 40 years (mean, 18). Ages varied from 31 to 69 years (mean, 55). The pulmonary fibrosis preceded the development of rheumatoid arthritis by one to 14 years (mean, 5.5 years) in six of the 16 patients and occurred after the development of rheumatoid arthritis by 10 months to 15 years (mean, 4.5 years) in 10.

All 16 patients complained of pain and stiffness in the involved joints and of increased fatigability. Fourteen complained of a dry cough and dyspnea on exertion; two had no pulmonary symptoms.

*Read at the meeting of the American Thoracic Society, Pittsburgh, May 21 to 24, 1967.

**Mayo Clinic and Mayo Foundation: Section of Medicine.

†See Test Your Word Score Page 1823.

All 16 had basilar rales on auscultation. One patient had clubbing of the digits; two patients had rheumatoid nodules at the elbow. The rheumatoid process involved hands, wrists, elbows, knees, and ankles. The degree of involvement varied from synovial thickening to destructive changes with rheumatoid deformities. There was no apparent correlation between the severity of the rheumatoid involvement and the severity of the pulmonary involvement.

Five of the 16 patients were tested for lupus erythematosus (LE) cells, and all tests were negative. Sedimentation rate, determined (Westergren) in all cases, varied from 16 to 105 mm. in one hour (mean, 54 mm.). The flocculation test for rheumatoid factor was performed in seven cases and was reactive in five. The serum protein electrophoretic pattern was determined in five cases; three showed increased globulin concentration (mean value, 2.3 gm/100 ml.). Sputum studies in all cases were negative for tuberculosis. Thoracic roentgenograms showed the typical nodular fibrosis in all 16 patients. Pulmonary function was studied in one patient and showed a restrictive and a diffusion abnormality. Lung biopsy (transbronchoscopic) in one patient disclosed interstitial pneumonitis with fibrosis and

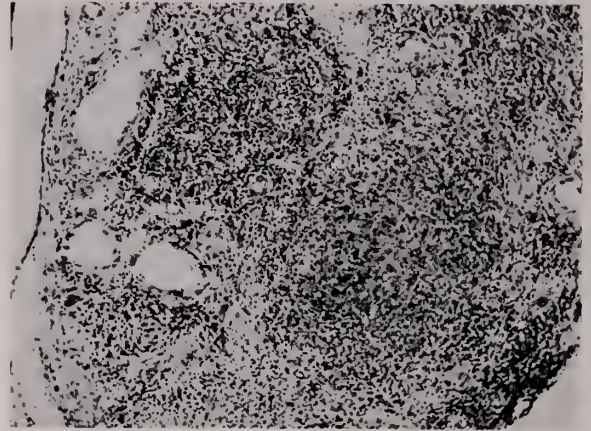


Fig. 1—Lung biopsy, showing interstitial pneumonitis with fibrosis. (Hematoxylin and eosin; $\times 75$.)

silica particles present (Figure 1). Open lung biopsy in a second case disclosed interstitial pneumonitis and nodule formation with central necrosis of collagen (Figure 2).

Case Report

A 49-year-old negro male welder was seen in August 1964 because of shortness of breath, dry nonproductive cough, pain with stiffness in the hands, wrists, and elbows, and increased fatigability. He had worked as a welder since 1951. A thoracic roentgenogram was described as abnormal in 1959, but an extensive work-up at that time, including scalene node biopsy, showed no other abnormality.

TABLE
Results of Pulmonary Function Studies

	Estimated normal	Found	Found after isoproterenol
Pulmonary volumes			
Vital capacity (expiratory), L	4.9	1.66	1.55
Inspiratory vital capacity, L	4.9	1.71	1.89
Residual volume, L	1.7	1.04	
Total capacity, L	6.6	2.75	
Res. vol./tot. cap. $\times 100$, %	<35	38	
Functional residual cap., L	3.0	1.40	
Expiratory reserve, L	1.3	0.36	
Max. breathing capacity, L/min.	115	49	60
Max. midexpiratory flow, L/sec.	2.5	1.3	1.7
Expiratory slowing, grade	0	3	2
Nitrogen washout index, % N_2	≤ 2.5	0.8	
Arterial O_2 saturation, % (oximeter)			
Resting (air)	95-98	96	
Resting (O_2)	100	100	
Before exercise (air)	95-98	93	
Exercise (air) for 4.1 min.	No fall	82	
Exercise (O_2) for 5.0 min.	100	100	
Ventilation (at sitting rest, breathing O_2)			
Liters per minute		12.42	
Respirations per minute		19.6	
Average tidal volume, ml.		633	

Physical examination revealed clubbing of fingers, synovitis of both elbows, and leathery rales at both bases posteriorly.

Laboratory data included normal values for blood hemoglobin concentration, leukocyte count, and urinalysis. The rheumatoid flocculation test (Hyland Laboratories) was reactive. A serologic test for syphilis was non-reactive, and the test for lupus erythematosus cells was negative. Sedimentation rate was 75 mm. in one hour (Westergren). A test with purified protein derivative, first strength, was negative, and one with the second strength was positive (2+). The protein electrophoretic pattern showed an increase in concentration of the globulin fraction (2.14 gm/100 ml.). Examinations of specimens of induced sputum, gastric washings, and bronchial secretions revealed no acid-fast bacilli. Hand and wrist roentgenograms were normal. A roentgenogram of the thorax showed a nodular infiltration with a reticular appearance extending throughout both lungs (Figure 3). Review of roentgenograms made elsewhere in 1959, 1961, and 1963 clearly showed a gradual increase in the pulmonary parenchymal infiltration since 1959. Pulmonary function tests (Table) showed a restrictive ventilatory abnormality with decreased carbon monoxide diffusing capacity (found, 9 ml/min/mm. Hg.; normal, 23 to 38).

The patient was instructed in breathing exercises and was advised to follow a regimen of prednisone, potassium iodide, and isoniazid.

Discussion

When Caplan described the association of nodular fibrosis of the lungs with rheumatoid arthritis in coal miners, he reported that 90% of 51 coal miners with rheumatoid arthritis showed more infiltration in the thorax than could be explained on the basis of pneumoconiosis alone. Progressive massive fibrosis also occurs in carbon-electrode workers,² boiler scalers,³ and workers exposed to the dust of iron, brass, sandblasting, and asbestos.⁴ The pulmonary lesions may not be associated with constitutional symptoms, and respiratory difficulty may be slight.⁵ There appears to be no relationship between the severity of the arthritis and the extent of the roentgenographic changes in the thorax.⁶ In most cases the onset of arthritis coincides with the development of the progressive fibrosis; in some cases, however, the characteristic roentgenographic appearance precedes the arthritis by several years.⁷

Gough and associates⁸ showed histologically that the essential difference between the orthodox pneumoconiotic nodules and the Caplan nodules was the presence of an inflammatory

reaction of the rheumatoid type in the latter. The characteristic lesion, consisting of fibrosing pneumonitis with necrobiotic* foci, bears a close resemblance to the subcutaneous nodules of rheumatoid arthritis. The central area of necrotic collagen is surrounded by an inflammatory cellular layer and a zone of fibroblasts containing multinucleated giant cells. The necessary factor for the production of these lesions seems to be the presence of collagen necrosis resulting from the reaction of sensitized lung to dust particles or to dust particles and tuberculosis. One theory has postulated that the fibrotic masses represent tubercular

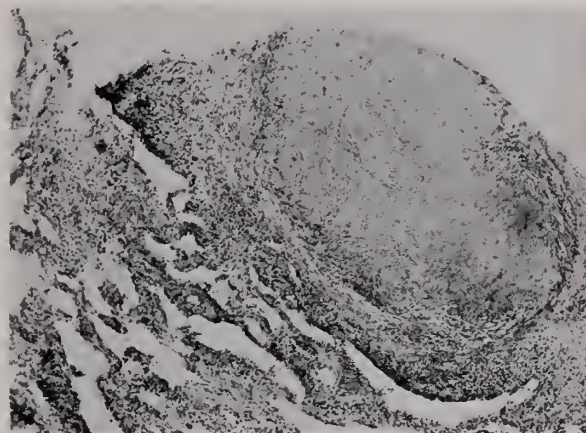


Fig. 2—Fibrotic nodule. Central area of necrotic collagen is surrounded by inflammatory cellular layer and zone of fibroblasts containing multinucleated giant cells. (Hematoxylin and eosin; x23.)

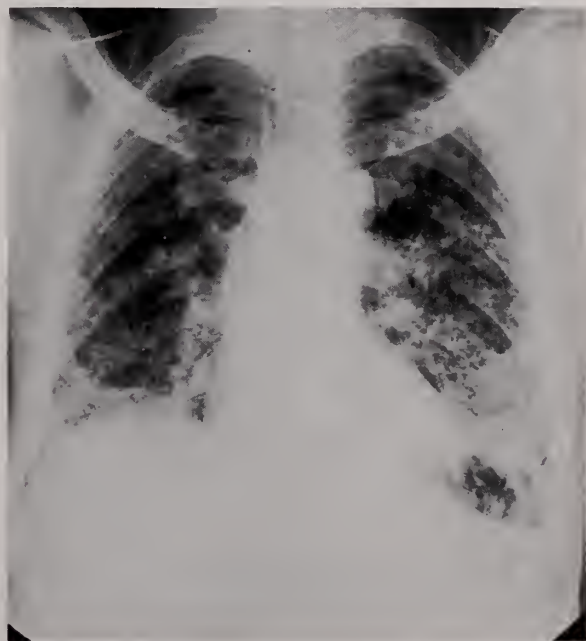


Fig. 3—Note reticular appearance throughout both lung fields, with nodular fibrosis bilaterally.

*See Test Your Word Score Page 1823.

lesions which have been modified by the presence of coal dust. There is little to support this contention because *Mycobacterium tuberculosis* cannot be demonstrated in the zones of active inflammation. The necrosis of collagen tissue is the fundamental change.⁸

The opacities in Caplan's syndrome are peripherally located, tend to be multiple, and usually affect both lungs. The lesions are similar in appearance to metastatic lesions. They appear rapidly but, once developed, remain unchanged for years. Many will show a mixed picture of round opacities, progressive massive fibrosis, and opacities indistinguishable from those of tuberculosis. Coal miners with rheumatoid arthritis react in a peculiar fashion to any collagen altered by the pneumoconiotic process. Possibly, the rheumatoid patient reacts to inhaled dust particles by means of an unusual hypersensitivity reaction which produces this characteristic picture. There is the possibility that these nodules are rheumatoid in origin and are exactly similar to the rheumatoid nodules commonly seen on the elbows in patients with active rheumatoid arthritis. It has been postulated that rheumatoid nodules develop because of trauma on the extensor surfaces and that they develop in the lung parenchyma because of antecedent damage from the dust particles. A patient with nodular rheumatoid lung disease, but nonpneumoconiotic, with extensive subcutaneous nodules and a positive LE cell test has been described.⁹

Treatment depends on the amount of disability from the pulmonary and from the joint manifestations. The treatment should be the same as for each condition when it exists alone. Irreversible pulmonary hypertension may be

delayed by appropriate treatment with steroids, which decreases the nodular fibrosis. One important aspect of treatment is the use of broad-spectrum antibiotics (tetracycline or ampicillin) with each infection of the upper respiratory tract to prevent a superimposed pneumonitis. Physical therapy, increased rest, salicylates, application of orthopedic measures when indicated, and attention to general health constitute the main treatment of the rheumatoid arthritis. Stronger antirheumatic medications can be used in selected cases.

In each suspected case of Caplan's syndrome, sputum and gastric washings should be studied to exclude active tuberculosis superimposed on a pneumoconiotic process. If steroids are used in the treatment, isoniazid should be administered prophylactically in a dosage of 300 mg. daily after breakfast if the tuberculin skin test is positive.

Summary

Sixteen patients with rheumatoid arthritis and nodular fibrosis of the lungs, seen at the Mayo Clinic in the 10-year period, 1955 through 1964, appeared to have the clinical syndrome, described in 1953 by Caplan, of rheumatoid arthritis with pneumoconiosis in coal miners. Awareness of the entity may prevent unnecessary studies for malignancy, including thoracotomy. The cause is unknown but it may be a hypersensitization reaction to irritating dust particles in the lung in rheumatoid patients, who already have an existing hyperimmune state. Caplan's syndrome may be not only a syndrome but an interesting corollary of the interaction between silicosis and hypersensitized tissues.

References

1. Caplan, A.: Certain Unusual Radiological Appearances in the Chest of Coal-Miners Suffering From Rheumatoid Arthritis. *Thorax* 8:29, 1953.
2. Watson, A. J.; Black, J.; Doig, A. T.; and Nagelschmidt, G.: Pneumoconiosis in Carbon Electrode Makers. *Brit J Industr Med* 16:274, 1959.
3. Campbell, J. A.: A Case of Caplan's Syndrome in a Boiler-Scaler. *Thorax* 13:177, 1958.
4. Rickards, A. G., and Barrett, G. M.: Rheumatoid Lung Changes Associated With Asbestosis. *Thorax* 13:185, 1958.
5. Caplan, A.; Cowen, E. D. H.; and Gough, J.: Rheumatoid Pneumoconiosis in a Foundry Worker. *Thorax* 13:181, 1958.
6. Miall, W. E.; Caplan, A.; Cochrane, A. L.; Kilpatrick, G. S.; and Oldham, P. D.: An Epidemiological Study of Rheumatoid Arthritis Associated With Characteristic Chest X-ray Appearances in Coal-Workers. *Brit Med J* 2:1231, 1953.
7. Morgan, W. K. C.: Caplan's Syndrome: An Interesting Clinico-pathological Occurrence. *Ann Intern Med* 55:667, 1961.
8. Gough, J.; Rivers, D.; and Seal, R. M. E.: Pathological Studies of Modified Pneumoconiosis in Coal-Miners With Rheumatoid Arthritis (Caplan's Syndrome). *Thorax* 10:9, 1955.
9. Robertson, J. L., and Brinkman, G. L.: Nodular Rheumatoid Lung Disease. *Amer J Med* 31:483, 1961.

Liver

A man's liver is his carburetor—Anon

Complete Heart Block*

An Experimental Study

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HEART BLOCK WAS first treated clinically by Weirich and others in 1957^{1,2} with an external pacemaker for temporary control of surgically induced heart block. Hunter and associates, in 1959, reported the use of a bipolar electrode.³ Chardack et al., in 1960, reported on the use of an entirely internal pacemaker with small cadmium-mercury batteries as a power source.⁴ Since that time over 5,000 units have been implanted. Beginning in 1962 with Dr. Edwards' help we began producing complete heart block under inflow occlusion.⁵ Stimulated by our interest in the conduction system⁵ we questioned whether it might be advantageous to attach at least one of the electrodes to the conduction bundle. This was done and gave an average 20% improvement in cardiac output in heart block over the usual attachment of both electrodes to the ventricular wall.⁷ In a study conducted to determine if this improvement was permanent we found that the intravenous pacer gave about 80% over-all improvement; but we had occasional difficulty with the intravenous pacer causing sudden ventricular fibrillation in the process of placement. In addition, after placement it tended to get out of control easily through simple changes of position or sometimes spontaneously. After surgically placing the intravenous pacer catheter tip in the right ventricular apex and fastening it with a suture, we observed 100% improvement over the usual external ventricular placement (Table 1).

Materials and Methods

In four dogs weighing 30 to 40 pounds the technique of cutting and then cauterizing the

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Pacemakers courtesy of Medtronic.

This investigation was supported in part by Public Health Service Research Grant 5 RO 1 H.E.-05694 from the National Heart Institute and in part by a Grant-in-aid from the Minnesota Heart Association.

conduction bundle in the right atrium under conditions of inflow occlusion⁵ caused complete heart block. After a month and with an intravenous pacer in place surgical anesthesia was induced with a 2½ percent solution of sodium pentothal injected intravenously. Assisted respiration was maintained with a mechanical respirator. In three animals the left fifth interspace was opened. In two, attachment of the pacemaker was to the ventricle and the conduction system. In one animal the usual ventricular attachment was used. In the fourth animal through a midline sternal splitting incision, an intravenous pacer catheter tip was placed in the apex of the right ventricle thru a small stab wound. Bleeding was easily controlled with a purse string suture which was also used to maintain the catheter in place. The attached pacemaker was imbedded in the muscle of the upper abdominal wall in all four animals. Cardiac outputs were determined using cardio-green dye and a densiometer^{6,7,8} at intervals of one to two months.

Values for cardiac output were converted to cardiac indices (cardiac output in liters/min./M²). For each study two and sometimes three determinations were done and averaged. Reproducibility of the determinations was within five percent. A total of 60 studies for cardiac output were done.

TABLE I

	Cardiac Output (L/min.)	Cardiac Index (L/min./M ²)	Percent Improvement
With Pacing two Ventricular Electrodes	2.8	2.1	
With Pacing one Conduction Bundle and one Ventricular Electrode	3.0	2.4	14%
Intravenous Pacer	4.3	3.8	80%
Apex Pacer	4.4	4.2	100%

Results

There was a persistent small improvement .3L (14%) with pacing using one electrode attached to the conduction bundle and one ven-

tricular electrode as compared to two ventricular electrodes (Table 1). The intravenous pacer when successful was much improved over both. The cardiac outputs converted to cardiac index for animals with the surgically implanted apical catheter electrode were about twice as good as for animals with epicardial electrode application and 20% better than the intravenous catheter (Table 1).

Comment

The experiments described indicate that implantation of the tip of an intravenous pacer into the apex of the right ventricular cavity gives the best cardiac output in complete heart block. It is probably reasonable to expect an improved contraction of the heart when the conduction bundle is stimulated by one electrode. Just why endocardial stimulation is so superior is not as clear. Perhaps it allows more rapid access to the conduction fibers just under the endocardium.

Summary

In four dogs with recently induced complete heart block three methods of pacing were compared with respect to index of cardiac output. In one dog the two electrodes were implanted in the ventricular wall. In two dogs one electrode was implanted in the left ventricular wall while the other was implanted in the conduction tissue distal to the level of the section which had been made for induction of complete heart block.

In one dog the tip of an intravenous pacing catheter was implanted in the apex of the right ventricular cavity and maintained in place by sutures in the myocardium. In all four dogs an intravenous pacing catheter was passed before surgery and studies done with this in place. The surgically implanted intravenous catheter in apex of the right ventricle gave the best results, averaging 100% better than when the electrodes were placed in the ventricular wall and 20% better than when the intravenous catheter was used.

References

1. Weirich, W. L., Gott, V. L., and Lillehei, C. W.: Treatment of Complete Heart Block by the Combined Use of A Myocardial Electrode and An Artificial Pacemaker. Surg Form 8:360, 1957.
2. Weirich, W. L., Paneth, M., Gott, V. L., and Lillehei, C. W.: Control of Complete Heart Block by Use of An Artificial Pacemaker and A Myocardial Electrode. Circulation Res 6:410, 1958.

3-8 May be secured from the author or the reprints.

Diverticulitis Complicating the Diagnosis of a Gynecological Malignancy

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SURGICAL CONDITIONS involving the female pelvis are not limited to lesions of the organs of reproduction. Acute appendicitis as a cause of right-sided pelvic pathology is well recognized. The differential diagnosis of lesions involving the left side of the pelvis should include diverticulitis of the sigmoid with or without abscess formation. In reviewing the English literature only one article³ points out this diagnostic problem.

Case Report

A 52-year-old-white female was hospitalized because of severe abdominal pain of two days' duration and vague abdominal discomfort and questionable bowel habit changes for the preceeding year. However, a complete physical examination including a pelvic examination and a barium enema nine months before had been normal. Prior to admission her diabetes mellitus had been successfully controlled for the preceding four years by oral antihyperglycemic medication which had followed an episode of acute pancreatitis. She had had some irregular vaginal bleeding following her menopause six years previously and there had also been a persistent serosanguinous vaginal discharge for the preceding one year.

At the time of admission due to abdominal pain her oral temperature was 102.4°F. Her hemoglobin, serum amylase, electrolytes and blood urea nitrogen were normal. The white blood cell count was 14,100 with 82% neutrophils. The blood sugar was 270 mgm %. Her urine was of high specific gravity with 4+ sugar and strongly-positive acetone.

Physical Findings

Her abdomen was flat with active bowel sounds. No masses or organs were palpable, but there was bilateral lower quadrant tenderness. The pelvic examination revealed a clear yellow fluid in the posterior vaginal vault, apparently originating from a red, friable, slightly necrotic cervical lesion which hid the external os. On bimanual examination diffuse pelvic tenderness was elicited. The uterus was enlarged, posterior in position and acutely tender. Microscopic examination of the cervical biopsy done on admission disclosed adenocarcinoma presumably of endometrial origin. The true pelvic findings were later clarified with an examination under anesthesia.

For the first six days of her hospitalization she had a

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febrile course in spite of antibiotic therapy. There was also considerable abdominal pain, requiring narcotics. Constipation was a particular problem. On her seventh hospital day she was examined and a uterine curettage was done under anesthesia. The uterus was probed to $7\frac{1}{2}$ cm. and was found to be anterior and to the right. A mass, approximately $5 \times 6 \times 10$ cm. slightly anterior to the uterus and moving freely with it, was palpated in the left adnexal region. On rectovaginal examination this mass filled the left side of the cul-de-sac. The moderate amount of friable tissue obtained from the uterus was adenocarcinoma, presumably of endometrial origin.

An intravenous pyelogram showed no abnormalities. The first barium enema disclosed an obstruction at the level of the junction of the descending and sigmoid colon. A second barium enema showed a fistulous tract leading to a small cavity at the area of the constriction (Figure 1). The distinction between a neoplastic and an inflammatory lesion could not be made. Sigmoidoscopy was normal to 16 cm..

At this juncture in her workup it was known that the patient had an adenocarcinoma in the uterine fundus that extended to the cervix. However, it was not known with certainty whether this represented a primary uterine tumor or a metastatic tumor with the primary in the ovary or the bowel. In either case there had to be an accompanying abscess secondary to invasion of the bowel wall by tumor. Although the possibility of diverticulitis of the sigmoid colon with abscess was considered, it was felt to be unlikely in view of the normal barium enema nine months prior to this illness. It was felt that an operation would offer the best possibility of a cure if this mass was a malignant tumor.

In consultation with the Surgical Service, a laparotomy was done. The surgical specimen included the lower por-

tion of the descending colon and upper portion of the rectum along with a total hysterectomy, bilateral salpingo-oophorectomy and a generous vaginal cuff. The aortic and pelvic nodes were also included in this en-bloc specimen. Upon dissection of the specimen an adenocarcinoma of the lower uterine fundus and a true diverticulum of the descending colon with abscess formation were found. The abscess was seen lying in the connective tissue between the uterus and colon. The patient tolerated the procedure well. Because of a large vaginal cuff, post-operative radiation was not given.

Discussion

It is impossible to estimate the frequency with which diverticulitis presents a diagnostic problem to the gynecologist. Hurwitz and Solomons,³ in their review of five cases of diverticulitis with abscess formation, found three cases with a preoperative diagnosis of twisted ovarian cyst and one case each with a diagnosis of ruptured ectopic pregnancy and of tubo-ovarian abscess. This error must occur with some frequency, because in most articles discussing surgical management of diverticulitis there are cases in which a laparotomy was done because of the mistaken diagnosis of a gynecologic problem. The lack of data regarding the true frequency of this problem can probably be attributed to authors' reluctance to publish their diagnostic errors.



Diverticulum of descending colon showing fistulous tract to abscess formation.

Undoubtedly diverticulitis often passes through a stage which can mimic a gynecological problem. By the fistulas that are formed, it can be seen that the organs of the female pelvis can be involved by diverticulitis when abscesses occur. This is not a common problem, however, and its rarity can be deduced from the following data. As late as 1957 only a third case of uterosigmoidal fistula due to diverticulitis had been described in the literature.⁵ Vaginosigmoidal fistulas, however, are thought to have an approximate incidence in diverticular abscess of 6.7% or less.^{2,6} Vesicosigmoidal fistulas occur four to five times more often in men than in women,⁴ probably because of the interpositioning of the uterus and its appendages between the bladder and sigmoid colon. Vesicosigmoidal fistulas do occur in women, however, with the approximate frequency of 2.0% of those patients with diverti-

cular abscesses.² This suggests that at least a significant number of diverticular abscesses involving the organs of female reproduction pass through a stage which could be suggestive of a primary gynecologic disorder. Once the fistula is present, however, the diagnostic error probably would not be made.

Many of the features of diverticulitis were present in this patient, but the presence of an adenocarcinoma of the endometrium and a normal barium enema study nine months before made the diagnosis of two separate entities seem ill-advised.

Summary

A patient with an adenocarcinoma of the endometrium and a concurrent pelvic abscess due to sigmoid diverticulitis can cause difficulty in differential diagnosis.

References

1. Brown, D. B. and Toomey, W. F.: Diverticular Disease of the Colon; A Review of 258 Cases. *Brit J Surg* XLVIII:485, 1960.
2. Hafner, C. D., Penka, J. L. and Brush, B. E.: Genitourinary Manifestations of Diverticulitis of the Colon; A Study of 500 Cases. *JAMA* 179:174, 1962.
3. Hurmity, Alfred and Solomons, Edward: Diverticulitis, A Diagnostic Dilemma; Report of Five Cases. *Obstet Gynec* 10:128, 1957.
4. Mayo, C. W. and Blunt, C. P.: The Surgical Management of the Complications of Diverticulitis of the Large Intestine. *Surg Clin N Amer* 30:1005, 1950.
5. Smalley, M. A., LoRusso, V. and O'Brien, J. E.: Sigmoidouterine Fistula Complicating Diverticulitis; Report of a Case. *JAMA* 165:827, 1962.
6. Zeigerman, J. H., Stahlgren, L. and Tulskey, E. G.: Sigmoidovaginal Fistulas; Review of the Literature and Report of a Case. *Amer J Obstet Gynec* 89:1003, 1964.

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Mr. President—Your Health*

Franklin Pierce—1804-1869

Healthwise Franklin Pierce's early life was uneventful until as a young congressman he yielded to social pressure to imbibe too freely. On one alcoholic spree he and his impetuous companions became involved in rough-and-ready fisticuffs with another group of roisterers. For young Pierce summary retribution followed the rash escapade; he was stricken with and thoroughly subdued by a severe attack of pleurisy. After two cupping procedures, removing first 16 ounces of blood and then 12, he improved and recovered; but for the rest of his life the memory of his youthful folly haunted him with remorse.

At the age of 42 Pierce joined the Mexican campaign as a brigadier general and while on the march westward contracted the insidiously prevalent army-camp intestinal infection with fever and diarrhea, an attack which prostrated and detained him for treatment and convalescence at Vera Cruz. When able, he rejoined his comrades in arms in time to participate in a dramatic military engagement: the Battle of Contreras. While advancing swiftly into action across a rough lava bed his horse shied, then tripped and tossed its rider onto jagged rocks, fracturing his pelvis and dislocating one knee. But Pierce scorned to abdicate to his injuries and retire from action. Instead, he contrived to mount another steed, upon whom he charged heroically into the fray, where he remained until late that night before he capitulated to pain and exhaustion. His recovery was slow and complicated by another assault on his weakened constitution by camp fever and dysentery.

During the succeeding civilian era of Pierce's life his health remained reasonably good except for recurring chest colds and chronic bronchitis, which may have been the precipitating cause of his reverting to overindulgence in alcohol, a habit he had never had sufficient moral stamina to overcome completely. But during this lapse from moderation a particularly severe attack of bronchitis galvanized him into a resolution to abstain permanently, a pledge he kept, while at the same time belatedly embracing religion.

During his later years Pierce was afflicted with chronic stomach discomfort and pain and finally dropsy and lethargy, terminating when he was 64 in a final sleep. The precipitating cause of death was never determined. Medical opinion included a number of pathologies: liver cirrhosis, stomach ulcer or tumor with peritonitis, perforated appendix: any one of these alone or in combination contributing to heart failure. No autopsy was held; the press laconically reported that death was due to "chronic inflammation of the stomach attended with dropsical effusion of the abdomen."

*With acknowledgments to Karl C. Wold, M.D.: Mr. President—How Is Your Health?

DERIVATIVELY SPEAKING

Pelvis—from Greek *pelyx* (wooden bowl)

One finger in the throat and one in the rectum make a good diagnostician.

—Osler

Every invalid is a physician.—Irish Proverb

Epilepsy in Children*

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ALTHOUGH EPILEPSY has been known in the human race for thousands of years it is only within the last 100 years that definite treatment and diagnostic procedures have improved. Five to six per cent of all children in the United States will have seizures before they are six years old, and most of these will be due to fever.

Principal Aspects of Epilepsy

It is important to rule out the possibility of all the unusual types of seizures. This we must do by dividing seizures into four major groups: grand-mal, the petit-mal and myoclonic types, psychomotor epilepsy, and the jacksonian** seizures (or in many cases a focal seizure, caused by cortical irritation).

The *grand-mal seizure* is generalized, and rather severe, usually accompanied by a cry or specific symptoms preceding the attack in children. Often stomach disturbances and auras of this type are followed by tonic and clonic movements and eventually by recovery and sleep. Usually these are not localized to one side of the body.

The *petit-mal and myoclonic groups* of seizures are relatively common in children. I have lumped these two together purposely because by electroencephalograph they show a close resemblance. The petit-mal or typical three-per-second high-voltage wave spike complex is rather characteristic of the momentary lapse or of the simple astatic or akinetic seizure (the seizure with the lack of movement). However, the myoclonic seizure is included in this group because of its appearance on the encephalogram; but it is, in my opinion, a very different kind of seizure, also responding to medication very differently. I feel that the electroencephalogram is sufficiently distinct in this particular group to help us to differentiate between the more specific forms of therapy, and for that reason I believe that the myoclonic seizure must, in as many cases as pos-

*Presented at the annual meeting of the Minnesota State Medical Association in Duluth, May 16, 1967.

**See Test Your Word Score Page 1823.

sible, be delineated by encephalograph and history of muscle-jerk seizures of a more generalized and less specifically tonic type than the characteristic grand-mal.

The *psychomotor seizures* were originally called "temporal lobe seizures," primarily because they involved, to a large degree, the function of speech, hearing, emotion and those autonomic functions of the internal viscera (nausea, salivation, vomiting, and symptoms involving the internal and visceral nervous system). These are important because basically they are difficult to treat compared to other types of seizures. They usually require *major* medication, and the prognosis is much more likely to depend upon the focus of the disorder and the cause, which may or may not be more ominous than those outlined above.

The *jacksonian or focal seizures* and those of the so-called localized cortical type encompass a variety of local seizures, often involving a very tiny portion of the body (in other cases a larger section) and the typical jacksonian march, beginning with one portion of the body and spreading to the rest of that side. Usually these seizures are unilateral and it is important to delineate them, because their category includes children suffering from birth injuries, brain tumors, angiomas or blood-vessel groups on the surface of the brain, scars, brain abscesses, and subdural hematomas (especially in infants under one year). These, of course, must first of all be considered in any seizure which *begins* in one area or which is localized or restricted to one area of the body.

Definitive Treatment

In the past, diagnosis has often been rather incomplete, and while most of us were taught in medical school that dilantin and phenobarbital were used for major epilepsy and tridione and paradione for petit-mal seizures, this is today an incomplete and insufficient classification for the specific and satisfactory care of the major forms of epilepsy.

The *grand-mal seizure* in its less serious forms may be cared for satisfactorily with Mebroin, dilantin or phenobarbital. I mentioned phenobarbital last because, except for those children who are brain-injured and require a stronger drug, Mebaral has been a

rather satisfactory drug for the standard school child and causes a distinctly smaller degree of drowsiness, irritability, and skin reaction than does phenobarbital.

The *petit-mal group of seizures* can be treated if separated, as mentioned above, into the petit-mal and/or myoclonic groups. The petit-mal group, primarily the "lapse" seizure or that involving a very minimal degree of movement or loss of either tone or body movement, usually is treated much more satisfactorily with the "dione" drugs, barbiturates, or Zarontin.

The myoclonic group is much more likely to respond to Mysoline, dilantin and, in many cases, also Zarontin. These three drugs may be combined for very severe cases of mixed myoclonic seizures. Mysoline and barbiturates should be avoided in combination since many children show a distinctly severe reaction involving sleepiness or evidence of a brain-stem depression when these drugs are used either in combination, or both combined with one of the other major drugs. The myoclonic seizure specifically involves a muscle-jerk component, and while it may be treated in combination with the "dione" or barbiturate drugs used in the more typical petit-mal seizure, more often than not the drugs used in major seizures will also be required. Psychomotor seizures usually require a combination of drugs used in major motor seizures, such as dilantin-Mysoline, dilantin-phenobarbital or dilantin and *both* of the other two drugs. In treating patients with epilepsy one should never forget the excellent results achieved in some patients by the ketogenic or high-fat diet using the ratio of three grams of fat to one gram of carbohydrate. This is a difficult diet to use. It requires careful co-operation between the hospital dietitian and the family and always a close liaison between the family and the physician. Properly used, with or without additional medication, a ketogenic diet has distinct advantages as well as some very pronounced limitations, such as keeping the child *on* it for any length of time. In the last two years a ten-day trial on Diamox has yielded good correlation with subsequent use of ketogenic* diet in small children. In some infants it also has been possible to use Diamox in the treatment of seizures where other drugs have been inadequate or the children

*See Test Your Word Score Page 1823.

have refused to eat the ketogenic diet.

Treatment of Febrile Seizures

Febrile seizures in children deserve closer attention than any other form of childhood epilepsy. This disease usually occurs between the ages of one and three years and generally takes place if the temperature is 103° or higher rectally. In children with brain damage the seizure may occur with a rectal temperature as low as 101°. Approximately two thirds of these children have an abnormal electrocardiogram and one half have a family history of siblings, parents, or close relatives having had febrile seizures in childhood. Usually the seizures are bilateral, but on occasions where there are some organic factors involved there may be a unilateral or focal component. This unilateral component occurring in a seizure with a temperature, however, is very suggestive evidence of brain damage in addition to the febrile seizure pattern.

Between 5 and 20% of these children will develop epilepsy of a non-febrile type at a later date. For this reason, we must consider, as does Dr. Livingston of Johns Hopkins University Medical School, that any seizure, whether

caused by fever or not, is epileptic and, if unchecked, may become more intense as well as more frequent. In the major types of epilepsy probably 50% of non-treated grand-mal seizures will eventually heal spontaneously, and 90% of the so-called petit-mal epileptics will be cured. As we become more aware of the sub-types of petit-mal seizures, the myoclonic type appears the more serious; it is often associated with brain damage and may be involved in a progressive type of deterioration with mental as well as physical aspects. For this reason it is important in *all* children who have seizures that the proper diagnosis and therapy be instituted and continued for four or five years.

Conclusion

Emphasis has been put on the proper differentiation of the sub-groups of the major epileptic categories and the application of proper medication to these types of seizures. It is important to treat the child at the very onset of the disease in order to minimize both the number of seizures and reduce the probability of recurrence at a later date.

Avicenna* on a Baffling Case

When in his flight from Mahmud of Ghazna he came incognito to Jurjan by the Caspian Sea, a relative of the ruler of that province lay sick of a malady which baffled all the local doctors. Avicenna, though his identity was then unknown, was invited to give his opinion, and after examining the patient, requested the collaboration of someone who knew all the districts and towns of the province, and who repeated the names while Avicenna kept his finger on the patient's pulse. At the mention of a certain town he felt a flutter in the pulse. "Now," said he, "I need someone who knows all the houses, streets and quarters of this town." Again when a certain street was mentioned the same phenomenon was repeated, and once again when the names of the inhabitants of a certain household were enumerated. Then Avicenna said, "It is finished. This lad is in love with such-and-such a girl, who lives in such-and-such a house, in such-and-such a street, in such-and-such a quarter of such-and-such a town; and the girl's face is the patient's cure." So the marriage was solemnized at a fortunate hour chosen by Avicenna, and thus the cure was completed.**

*See Test Your Word Score Page 1823.

**Edward Browne: Arabian Medicine.

Despise no new accident in your body, but ask opinion of it.—Bacon

Wherever a doctor cannot do good, he must be kept from doing harm.

—Hippocrates

John Hunter's Menagerie

Before going off to war, John made plans to start a menagerie for the study of all kinds of animals. He had leased two acres in Earl's Court in the village of Kensington where he proposed to build a house for his collection.

The design of the house was as unique as the idea of the menagerie was unorthodox. Over the door hung the head of a crocodile with gaping jaws. Four life-size statues of lions, two rearing and two crouching, were set on each side of the building. Back of the house was a den where real lions and leopards were chained. Over the den there was a mound of earth, topped with piles of seashells, in the shape of a little fort on which was mounted a small gun.

The strangest sight was the barnyard. Here all kinds of domestic and wild animals roamed in confusion. Rare birds and serpents, ostriches, geese, and pheasants mingled with buffalo and deer. Fowl with human teeth grafted on the combs, hens with roosters' feathers, goats and dogs were all there for some type of experiment. In a small fishpond Hunter bred eels, leeches, carp, and river mussels. Hedgehogs and other hibernating animals were kept in burrows to yield their secrets of winter sleep. No specimen was too bizarre for the surgeon-scientist to scrutinize. There were goose eggs for the study of embryology, pond water for fresh-water life, the skeleton of a giant dancing bear contracted for with a traveling gypsy when it was alive.

He frequented the pet shops, looking for strange creatures, and begged zoo keepers and members of expeditions for any rare beasts they might encounter. Dead animals were useful, too. Certain parts he pickled in jars, others he dried. The rest were boiled down in a copper vat and the skeletons preserved.*

*Sarah R. Riedman: *Masters of the Scalpel*, 1962.

Autology

E. R. Moras, M.D., founder of Autology, finally arrived in the "booby-hatch." Before that, however, he had achieved a considerable following through advertising in the press, and through exploitation along the lines established by Elbert Hubbard.

Autology is a system of stereotyped hygienic and dietetic advice sandwiched in between a lot of pseudo-science and bad counsel. It is essentially another preachment of Ecclesiastes' urge for moderation in all things. Unfortunately it was carried to the point at which Elbert Hubbard said, "Moderation, equality, work and love—you need no other physician." Moras exploited his book at anywhere from \$10 to \$2, and on the side sold some patent medicines. Finally, his eccentricity went beyond the bounds of legal sufferance. He was arrested for insulting a woman on a train; he attempted to blackmail Leon Mandel out of a million dollars, and appealed to the President of the United States to help him collect \$50,000 from Parke-Davis and Company. So his friends put him in a sanatorium.*

*Morris Fishbein, M.D.: *The New Medical Follies*, 1927.

Heredity

A man is the sum of his ancestors; to reform him you must begin with a dead ape and work downward through a million graves.—Ambrose Bierce

Communication between Parents and Child

A Pediatrician's Viewpoint

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ALTHOUGH PHYSICIANS have long been interested in the emotional relationships between parents and child and the child's adaptation to his environment, recent years have seen more emphasis in this direction. This heightened interest has come about for three reasons: 1, the relative decrease in certain types of childhood diseases, 2, the growing sophistication of mothers and their familiarity with problems of rearing children, and 3, the affluence of the present generation and the Great Society programs, tending to extend the scope and depth of medical care for children.

American mothers have become increasingly concerned with the emotional health of their children, relying on the physician to advise on a host of psychologic issues, from simple matters of child care to problems of behavioral disturbance, weaning, toilet training, and discipline.

Communication

"Communication," derived from a Latin root meaning "sharing," implies a total projection of one's thoughts and feelings, whether by words or action, on the one hand, or on the other, by a deficit of transmission. The more intimate the relationship the better the communication.

Physicians are inclined to regard communication as verbal and forget the equally important, nonverbal signs that communicate as effectively as the spoken word. A glance, a sign, a smile, a wave, a sneer, a smirk, or a grunt, and even stony or impassioned silence convey ideas or feelings. The same words may even be made to have different meanings by the speaker's inflection. In fact, words may not even be necessary. Recently Sorenson and Gajdusek¹ described a type of communication by extraordinary and extravagant eye gestures used among primitive tribes in New Guinea.

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The goals of communication are *first*, the promotion and establishment of a personal relationship and, *second*, the transmission of information. Communication is a learned or acquired ability, of which speech is the most direct form. Communication has been called the currency of social structure. Dr. M. Robert Wilson, Jr.,* states that without communication man becomes psychotic and withdraws into himself. Communication is to the mind and soul what oxygen is to the tissues. In humans communication has reached the highest level. Electronics has augmented and facilitated communication but has not changed it, in that one man still has to convey his thoughts to another.

The consideration of communication between children and parents is divided according to three age groups: the infant and toddler, the "middle-aged" child, and the adolescent. Each group will be considered in a separate section. A fourth section is about parents.

The Infant and Toddler

At birth the infant suddenly changes his environment from a warm, silent, liquid medium to a world full of sights, smells, tactile sensations and sounds. His potential for responding to his new world consists of the simplest and most primitive of reactions. Perhaps the first significant communication he receives is the comfort and pleasure of being held by his mother. He communicates in turn, becoming completely relaxed in her arms, but anxious, struggling, and vocal in the arms of some other person.

In a matter of days or weeks he learns to communicate his feelings of tension or relaxation. He associates comfort, satisfaction, and relief of tension with his mother. He develops trust in her and a growing sense of his importance to her because she attends to his needs. Failure of an infant to learn trust because of a failure in the development of trust in the mother or a mother figure brings a breakdown in communication and causes him to withdraw into a world of his own. Such an infant is emotionally deprived.

*I am indebted to Dr. Wilson, Consultant in Child Psychiatry, Mayo Clinic, for his suggestions and encouragement in the preparation of this manuscript.

Tension

Some infants are considerably more hyperactive than others. Such an infant displays his tensions by screaming, rooting about, waving his arms and legs, and exhibiting much more than average wakefulness. The "colicky" infant is the infantile personification of tension. He generates considerable anxiety in his parents; on the other hand, sometimes anxiety in the parents generates colic in the infant; thus the whole family is affected. Colic appears to be a physiologic state affecting certain infants for a limited time. It is not caused solely by a nervous or anxious mother but represents an interaction or a two-way communication between mother and infant. A mother may become angry with an infant and may not be able to cope with these feelings unless she discusses them with a physician; or she may become frustrated by the demands he makes on her. Her feelings of anger, unless they are understood and discussed by physician and mother, may be harbingers of future difficulties.

Confidence

As a toddler, the child develops physical skills, greater strength and improved coordination, confidence, and some independence. He asserts this independence in positive ways such as demands for various objects or actions and also in negative ways in the form of resistance. The mother now becomes concerned with discipline, although unaware that she has been applying it in its simplest form from early infancy.

Discipline

The word "discipline" means to teach, and the mother has been teaching the infant through words and nonverbal communication when she has approved or disapproved of his behavior. He may have resisted being put back in the crib or have manifested likes or dislikes for foods; yet his mother has communicated to him that his behavior must be modified. The later disciplines the mother exercises are less subtle, such as the insistence that the child not handle certain breakable objects about the home, that he stay away

from the steps, or that he remain in the yard and not run into the street. It may be necessary to scold him or spank him to emphasize that he must comply with the family rules for acceptable behavior.

Acceptance

The attitudes of his mother, father, and siblings communicate to him acceptance of or dissatisfaction with his activities. Family members do not yield to every whim or tolerate every activity merely because he is an infant; yet their intolerance does not constitute rejection. Communicated to him are loving attitudes and acceptance, whether he has merited praise or disapproval. Anger on the part of either the child or the parents has long since entered into the relationship. The child may display anger because he has been denied something or been compelled to do something. His natural reluctance has to be expected and understood and tolerated to a point. Anger in the parent may be an appropriate reaction if the child is impressed that something will be demanded of him. Parents must realize that anger is a justifiable and appropriate reaction. They must also be aware of the purpose for the anger—that it is a reaction to an action on the part of the child rather than anger toward the child himself. The child has to learn that his anger or a parent's anger is acceptable and need not necessarily hurt, be ugly, or be destructive.

Fear

A child misbehaves as a result of aggressive and hostile impulses, and a too punitive approach by the parent may threaten him so greatly that he withdraws in retaliation never to attempt his actions again. In such circumstances the lesson he learns is one of fear rather than one of correction or education.

Dr. Stella Chess² has risen to the defense of mothers by stating that the response of a child to a parental approach in various areas and at different ages is determined not only by the attitude of the parent but by the child's own temperament. In other words, the mother must not be blamed for problems in the child, since in the complex parent-child reciprocity every action has an equal and opposite reac-

tion. The response of a child to a parent depends just as much on the child's own characteristics of reaction as on the parent's characteristics or on the manner in which the parent applies the communication.

Family Unity

During the toddler and preschool age there are often two main sources of anxiety for parents: eating habits and toilet training. Since the child after infancy enters a phase of reduced growth rate he has a reduced need for food; consequently his appetite is capricious. His parents may regard the amount of food he eats as insufficient for the maintenance of good health and become anxious. This anxiety is often a result of misinformation or folklore and sometimes is a carryover from their own childhood. Since it has been shown that malnutrition is not likely to occur in a child who has no metabolic defect and to whom adequate food is available, supplemental vitamins are seldom necessary beyond early infancy. I would like to regard the family dinner table as a sort of family forum where each one can catch up on the activities of the others during the day. I would cast my vote for preservation of the family dinner hour as essential to interpersonal communication and a sense of family unity.

Toilet Training

Toilet training of the child often depends on the whims of his mother, the amount of experience she has had with previous children, and the amount of resistance offered by the child. It may even be influenced by the mother's own childhood experience. The child often knows what is expected of him but may not be able to accommodate his mother with the hoped for evacuation when he is placed on the potty-chair. Too often she communicates her dissatisfaction, or at times her elation if the child is able to perform.

Little is to be gained in the long run and sometimes a great price may be paid for too early attempts at toilet training. If training is delayed until the child indicates that he prefers to have dry pants and betakes himself to the toilet, the end result will be much more satisfactory. On the other hand, the child who is compliant and performs each time he is set

upon the stool may undergo a change of heart at four, five, or six years of age and begin to retain feces, to wet or soil, or to do both sometimes.

Erikson³ has commented on identification of child with parents. He makes the point that individuals like Hitler and Gorky received little mother love and suffered under a tyrannical father (or grandfather, in Gorky's case). In situations where the child has no satisfactory and warm relationship with either a mother or a father, reactions in the course of personality development can be expected to differ from the norm. A boy who has no satisfactory identification with his father because the father is an inadequate individual, failing to fulfill the role of either father or husband, can hardly be expected to have a satisfactory opinion of his own father and perhaps even of men in general. If his mother fails to fill her role as a normal mother but is either tyrannical or, on the contrary, possessive or smothering, his relationship to women and his estimation of them are affected significantly, sometimes throughout life. Obviously, an environment of love produces individuals capable of love, and one of tyranny is apt to beget tyranny.

The "Middle-Aged" Child

One of the delights of the "middle-aged" child is his growing independence. He is able to dress himself, feed himself, and attend to his own needs. His world is expanding outside the home, and it is normal for him to spend a fair amount of his time away from home. However, this is not ordinarily a source of great concern to the normal parent.

The Anxious Parent

The physician should be concerned about the parent who is anxious or the child who is anxious because of time spent away from home. The basis for anxiety should be discovered and the emotion dispelled. This period of childhood is notable for other behavior, though it may be of only very temporary concern to the parents: specifically, lying, stealing, facial grimacing or tics, and occasional outbursts of independent action. The physician should *caution parents to be aware lest*

they prejudge, convict, and sentence a child before the evidence has been examined and the defense heard. Normally a parent does not immediately conceive of the child as growing up to be a criminal on the basis of a few stolen pennies or some small episode of lying. A child is apt to lose his repentant feelings when he is guilty, if his parents accuse him and then refuse to listen to the facts. Therefore the child, rather than feeling repentant, turns his indignity to anger and resentment.

Home Work

Another difficulty that may arise during this phase in child development is poor scholarship. I have often wondered whether these school problems are not aggravated, perhaps even fostered, by homework. *Educators are fairly well agreed that homework is merely busy work and contributes little toward the education of the child during these early school years.* Parents should take the attitude that schoolwork is given for the child and not the parent and that it is the child's responsibility. He should be left to his own devices and suffer the consequences if he fails to complete his assignments. When poor grades or failures occur, a parent must be careful not to consider the child's failure a parental failure. If the parent takes this as a personal failure, much emotional reaction is generated and often directed toward the teacher. Instances of underachievement in school are usually not due to lack of intellect in the child but rather to lack of motivation, this more often being the result of too much rather than too little parental pressure.

Parental Attitude

The parent must be careful that a reaction toward a child's poor school performance does not communicate to the child the notion that he is inferior and perhaps even willful in the failure. Motivation cannot be demanded; it is more like inspiration and is communicated only through proper parental attitudes, principally patience, understanding, and support rather than through threats, punishment, cajoling, or bribery. Parents often set goals for the child which they themselves failed to attain. Scholarship surely does not flow from homes

where parents have no scholarly values. Too much attention to the sports pages and television and a lack of books in the home are testimony to a parent's attitude regarding intellectual pursuits. Neither can scholarly parents force a scholarly attitude on children. *The child is a great imitator* and, if allowed to direct his own activities with the counsel of understanding parents, he will make the most of his intellectual endowment and be happy in it.

The parent who has had trouble with teachers during his own childhood, perhaps through misbehavior, truancy, or academic failure, may have difficulty preventing these attitudes from being communicated to the child. Often parents sabotage the efforts of teachers by their reaction to what goes on at school. The confusion that this may produce in the child is obvious. Parents may preach about the value of education, yet may sabotage the efforts of the school by berating the teachers or the system. Parents should be aware of a common practice of exploitation of their children for their own gratification. A brilliant performance at a recital or on the athletic field is laudable, but only if it represents initiative and accomplishment on the part of the child without pressure from the parent. Paper routes, lawn mowing, snow shoveling, and other chores are all worthwhile endeavors for the child, provided the job seems to be a good idea to him. A parental decree about jobs for the pre-adolescent is loaded with potentially unpleasant or even dangerous reactions. Parents should be aware that the child's welfare is paramount*; otherwise reasonable resentment toward the parent from the child will be the consequence and the end result unsatisfactory.

"Fostering"

The late Dr. Adelaide Johnson⁴ frequently commented on "fostering" as a factor in misbehavior of children. The inability to set definite limits and to establish definite prohibitions when a child has transgressed is in effect fostering. When a child misbehaves or, on the contrary, fails to do what he has been told to do and parents do not make their disapproval known in definite terms, they are guilty of fail-

ing to establish definite prohibitions. There may be situations in which parents express, in horrified tones, their shock and disapproval of what the child has done, but unless they really feel and express sincerely (communicate) that they do not approve and furthermore that the action will not be tolerated again, they have failed to transmit to the child the right concepts, because they themselves do not have these convictions. In brief, they are phoney as parents if they say one thing and yet lack conviction themselves; they are phoney if they demand one thing and tolerate another in terms of child behavior. Dr. Johnson once recounted an episode in which a child ran away from home and was punished for it; yet the parent obviously obtained a great deal of vicarious gratification from having the child recount in great detail where he had gone, whom he had met, and what he had done. By such a parental reaction, permission was conveyed though prohibition was voiced. *Sometimes parents may foster lying if they try to get a child to lie by asking questions that they know may demand his lying.*

Another common parental injustice is backing a child into a corner from which there is no dignified escape, except by total surrender and indignity.

As the child grows older it becomes obvious that parents, good or bad, increasingly communicate their integrity or lack of it through everything they do or say.

The Adolescent

Adolescence has been termed the age of noncommunication. Actually it is not a phase of noncommunication, but rather a phase of a different type of communication. The adolescent does not often confide in parents as to his thoughts, objectives, and experiences; but if he is observed closely by a considerate and understanding parent, his action and dress will belie his emotional states. *Adolescence is a stormy mountain pass between two tranquil valleys*, childhood and adulthood. The adolescent's world is more turbulent; his behavior traits are reflections of his bodily changes, his sexual awareness, and his questioning of authority. Though the adolescent challenges authority, he needs it and feels anxious and insecure without it. He is often moody, solemn,

*See Test Your Word Score Page 1823.

aggressive, and hostile toward parents and even toward visitors, the latter hostility often intended to embarrass his parents. However, outward signs of inner turbulence need not be considered pathologic. This inner turbulence is reflected in the type of music he enjoys, in sports, in hobbies, and in the "go-go" way he launches himself into activity. For some reason or other, parents who considered themselves adequate while the child was in the earlier phases suddenly seem to be inadequate, and many lose their self-confidence, temporarily if not longer.

The Disillusion of Hypocrisy

Unfortunately, parents often are guilty of a sermonizing monologue: they lecture the adolescent on honesty and good morals; yet they themselves may receive tickets for speeding, may drink to excess, or may behave toward a spouse in any but an exemplary manner. Adolescents are not deceived by hypocrisy but they are disillusioned. Parents should be consoled by the thought that most adolescents have the strength to weather the difficulties of this period. If parents can retain their "cool" and be cautious lest some of their disapproval and reaction provoke adolescents into rash behavior, things will gradually work out.

Antisocial Behavior

Parents should be more concerned if the adolescent shows preoccupation with physical development, anxiety over the sexual role, a paucity of rebellion, excessive shyness, antisocial behavior, sudden or gradual loss of interest in environment, excessive feelings of guilt, and failure in school. Often during these difficult periods the parent needs more guidance than the adolescent. The adolescent is gradually able to work out his emancipation from dependency on parents if the father or mother does not make this more difficult by being too possessive, domineering, or demanding. While the adolescent is being encouraged to mature, to form personal convictions, and to chart an independent course of action, his achievement of these various characteristics often threatens a parent and brings about parental disapproval or denial toward the adolescent.

Characteristically, the adolescent is disorderly in his room. Magazines and clothing are strewn about. Dirty clothes remain under the bed. Radio or record players blare loudly. Even such simple personal habits as brushing the teeth are often neglected, yet on the contrary the hair may be shampooed daily and the cologne may be applied to the point of near asphyxiation for the rest of the family. The adolescent behaves as at least two different persons. He may present one face to his family and yet another to his friends. But are not parents themselves guilty of such complex performances? May not they present one face to the family, another to their colleagues, perhaps another to their subordinates, and still another to their superiors?

The adolescent is apt to set king-sized goals for himself—goals that can hardly be attained by his pint-sized efforts. He may have ambitions to be a great athlete or musician, but he cannot be bothered with the discipline of practice. An adolescent begins to attain his real identity when he no longer pursues goals that he cannot realistically hope to reach.

With the Group

Though parents may think that adolescents are radical because of their dress and general appearance as well as their behavior, adolescents are actually conservative in that they do not want to be regarded as different from their peers. The emotional struggles over masculine and feminine strivings, over aggressivity or passivity, are apparent in boys in the long-pointed high-heeled shoes, the curling hair, the long sideburns, and the toiletries. Most of these adolescents want to remain with the group because they thereby avoid personal responsibility and perpetuate their emotional dependency, not on parents but on the crowd.

Often it is possible to understand adolescents better by studying their dress. Easson⁵ has stated that girls seem to be one or two years ahead of boys in establishing identity. A young man struggling with rebellious and aggressive urges proclaims his feelings in reds and in garish dress, the girls in pinks and yellows. The appearance of overneatness and fussiness in clothing, hair styles, and general appearance may suggest rigid compulsiveness. Anxiety may be represented by disarray and disorgani-

zation of the adolescent's dress. Some parents have noted that adolescents have worn "upset clothes," or "runaway shoes," or a black T-shirt when things are going wrong for them.

Parents are not wise when they go to extremes to keep peace in the family. Often a blowup does an adolescent good. It gives him a chance to get rid of feelings bottled up inside that make him restless and discontented and generally hard to get along with. However, parents should be cautioned to be careful about provoking adolescents into a blowup which may stampede them into taking an unreasonable course of action that will have rash or bitter consequences.

The Parents

Missildine⁶ has stated that emotional problems in the child are a reflection of the pathogenic nature of the attributes of his parents. These emotional problems are intensified when parental attitudes interact to create an atmosphere of conflict in the family. Normally there is an emotional interchange between husband and wife, but when conflicts are deep and prolonged they institute what is referred to as a marital problem.

The parent's view of a child often becomes skewed and distorted because of his own conflicts; then the child becomes a pawn, his allegiance a goal in the marital war, or a weapon to be used by one partner against the other.

The chief difference between children and adults is that children have parents to guide and instruct them and to create the emotional atmosphere in which they all live. Though many persons come from homes where their parents treated them as individuals and with firm and uncritical limits and where a mutual atmosphere of respect prevailed, some are not so fortunate. Their parents did the best they could; but being only human, they had problems that distorted or prevented their regard for and treatment of their children. When such children become adults, they are guilty of these same errors. They tend to recreate in-

side themselves the atmosphere of their childhood homes.

It is apparent that the total quality of each parent is communicated to the child genetically or through living together. One's integrity is on the line. The role of a conscientious and loving parent requires continual self-improvement. If, as an adult, he tends to be distrustful, suspicious, easily tempted to minor infractions such as cheating the grocer or sending the over-aged children to the theater for half price, he can expect the same set of values in his offspring. If husband and wife feel little respect for each other, as reflected in speech or attitude, how can they expect to inculcate a different set of values in their children? Temper tantrums, dish throwing, and cursing are just as immature for adults as for children.

Although adolescents seem to bicker and to harangue one another, they are nonetheless deeply affected by parental disagreement because it rocks the very foundations of their own security. They have parents on a pedestal, and to see a parent fall from a place of respect is a crushing blow not easily overcome. On the other hand, differences of opinion handled in a mature fashion convince the adolescent that some minor problems are a part of normal family life and that resolution may be accomplished without serious consequences.

As physicians we can reassure parents that their role as parents is probably the greatest challenge that life will present. It is one continuous struggle with new adventures; but it is never dull despite frustrations, disappointments, and few triumphs. It is exacting because it demands continual self-improvement and sacrifice. The gratifications come not as great and solemn events but as little experiences and an occasional awareness of a job well done. For the conscientious parent, rearing children is not just a hobby or a spare-time job, but rather a total investment of self. Whereas spoken and printed words may be the commodities of communication for the outside world, the actions of parents are the most eloquent means of communication as far as the family is concerned.

References may be secured from the author.

As scarce as truth is, the supply has always been in excess of the demand.
—Josh Billings

It Was a Family Tradition

Father used the spare bedrooms in the house for performing operations such as would be done today only in a hospital, with every conceivable equipment to hand and assisted by trained anesthetists and nurses. He did these as a matter of course, and mother helped him, also as a matter of course.

Naturally I wasn't present when father removed the tumor from Minnie Fenstermacher, but I am certain that in spite of his crude instruments and limited facilities it was done so deftly as to have earned the respect of a modern surgeon—and a little awe, as well, at his success under those conditions.

The patient stayed for a couple of weeks to recuperate, nursed by mother and tended by Abbie. The tumor, a fatty, fleshy growth, considerably larger than a baseball, was put in a tub of water and set on the second floor back porch until father would have an opportunity to put it in alcohol and add it to his collection of similar trophies of the operating table.

Neither he nor mother knew, of course, that their youngest son spent a happy, six-year-old afternoon at a new diversion. I had gotten a long shingle from behind the barn and split it so as to make a nice bat. With this I played a game all afternoon, hitting the tumor back and forth across the tub.

It was natural, therefore, that I should feel destined for medicine. All my play was of doctors and hospitals. My favorite patients were dogs, and by the time I was nine or ten I had established on the second-story back porch a regular hospital for all the stray animals in town.*

*Lewis R. Tryon (1872-1951) in *WHY WE BECAME DOCTORS*, edited by Noah Fabricant, M.D., 1954.

Note: Lewis Tryon served in World War I, being decorated by the Estonian and Latvian governments. Later he served with the Veterans Administration.

Bone Grafts on the Frontier

An operation performed by a Texas doctor, C. W. Truehart, was a striking demonstration of frontier medical skill. A young man had received the full blast of a shotgun in his left shoulder at short range. Cleaning the wound of gun wadding, fragments of clothing, and shot, the doctor applied skin grafts. The wound finally healed except for the clavicular region where a three-inch gap in the bones allowed the shoulder to droop.

Dr. Truehart rounded up a collection of healthy dogs. Nine weeks later he removed the granulation tissue, and between the ends of the youth's bones he inserted small periosteum and bone grafts taken from the dogs, which he chloroformed for the purpose. Eight out of ten grafts took. In two months the incision was healed; the clavicle was the correct length, and the shoulder did not droop.*

*Richard Dunlop, M.D.: *Doctors of the American Frontier*

Friendship lives on its income, love devours its capital.

—Arsene Houssaye

If you make people think they're thinking, they'll love you; but if you really make them think, they'll hate you.—Don Marquis



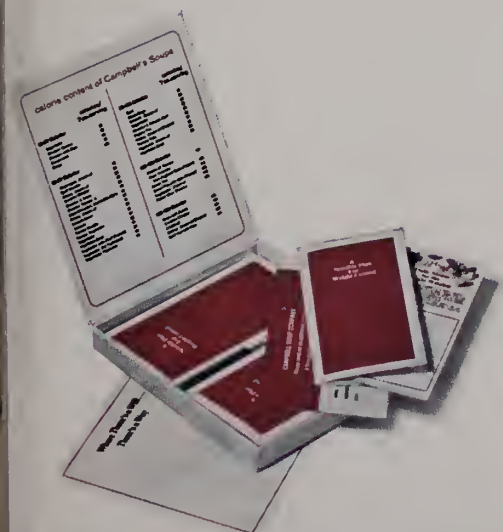
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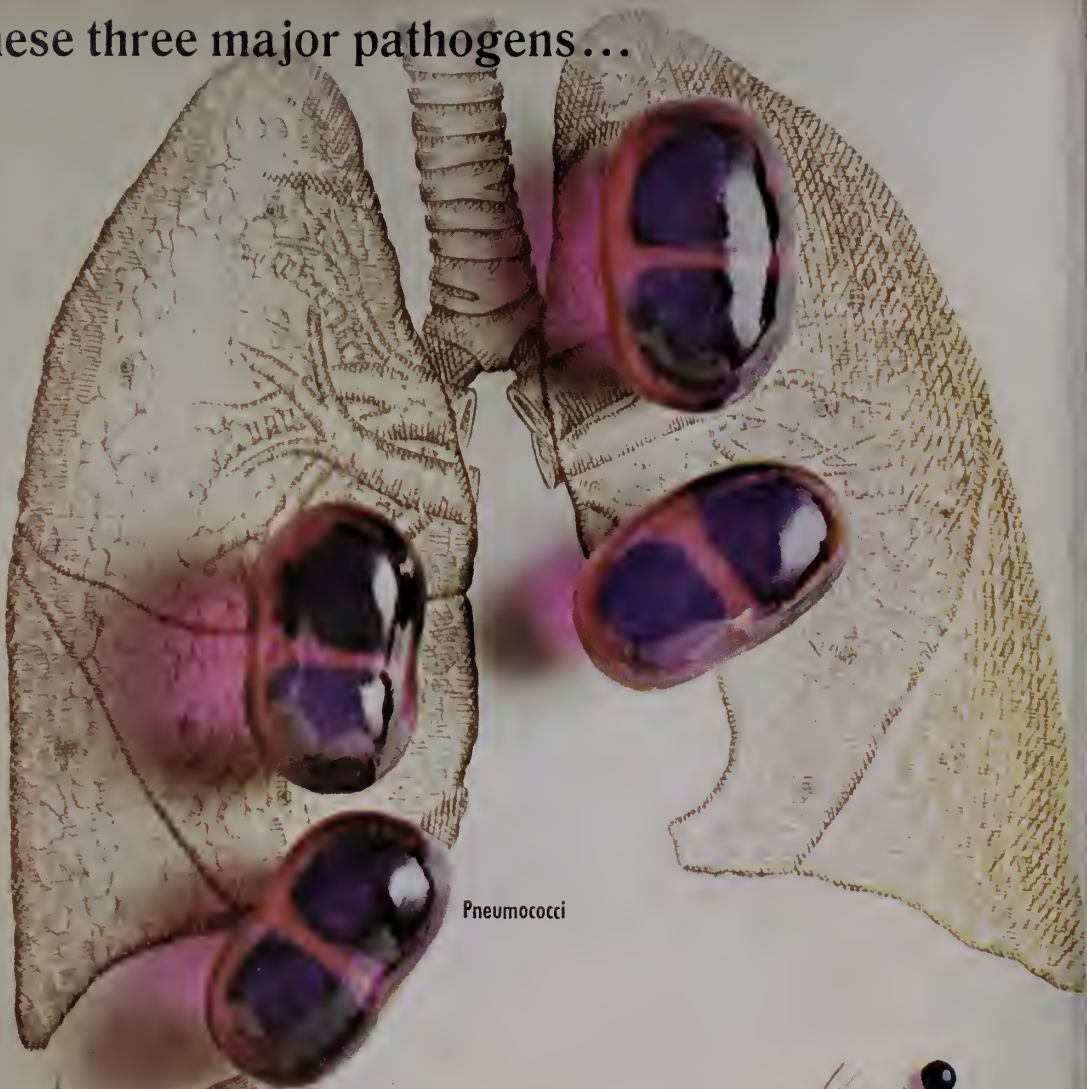
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One rounded teaspoonful of Metamucil powder in a glass of cool liquid, or one packet of Instant Mix Metamucil in a glass of water. An additional glass of liquid is helpful.

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V-Cillin K is stable in acid and immediately soluble. High serum levels, therefore, are reached rapidly. Because it is acid stable, V-Cillin K is well absorbed even when taken close to mealtime. These desirable properties help make V-Cillin K a dependable penicillin for oral use.

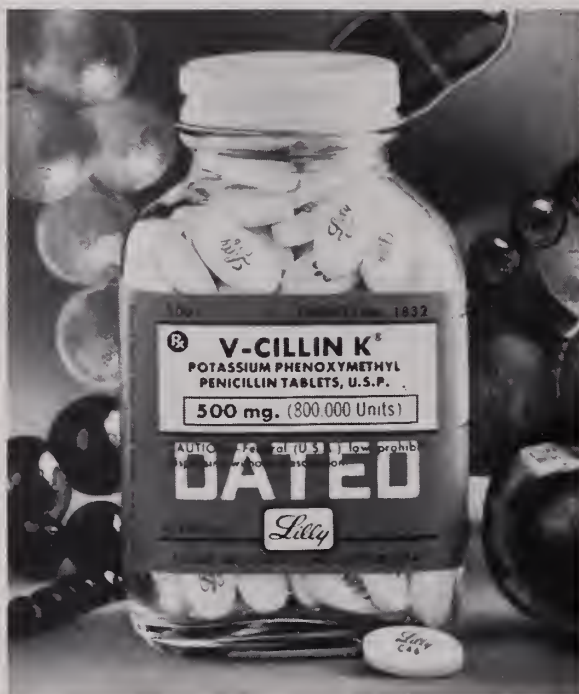


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Indications: Streptococcus, pneumococcus, and gonococcus infections; infections caused by sensitive strains of staphylococci; prophylaxis of streptococcus infections in patients with a history of rheumatic fever; and prevention of bacterial endocarditis after tonsillectomy and tooth extraction in patients with a history of rheumatic fever or congenital heart disease.

Contraindication: Penicillin hypersensitivity.

Warnings: In rare instances, penicillin may cause acute anaphylaxis which may prove fatal unless promptly controlled. This type of reaction appears more frequently in patients with a history of sensitivity reactions to penicillin or with bronchial asthma or other allergies. Resuscitative drugs should be readily available. These include epinephrine and pressor drugs (as well as oxygen for inhalation) for immediate allergic manifestations and antihistamines and corticosteroids for delayed effects.

Precautions: Use cautiously, if at all, in a patient with a strongly positive history of allergy.

In prolonged therapy with penicillin, and particularly with high parenteral dosage schedules, frequent evaluation of the renal and hematopoietic systems is recommended.

In suspected staphylococcus infections, proper laboratory studies (including sensitivity tests) should be performed.

The use of penicillin may be associated with the overgrowth of penicillin-insensitive organisms. In such cases, discontinue administration and take appropriate measures.

Adverse Reactions: Although serious allergic reactions are much less common with oral penicillin than with intramuscular forms, manifestations of penicillin allergy may occur.

Penicillin is a substance of low toxicity, but it possesses a significant index of sensitization. The following hypersensitivity reactions have been reported: skin rashes ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; and reactions resembling serum sickness, including chills, fever, edema, arthralgia, and prostration. Severe and often fatal anaphylaxis has occurred (see Warnings). Hemolytic anemia, leukopenia, thrombocytopenia, and nephropathy are rarely observed side-effects and are usually associated with high parenteral dosage.

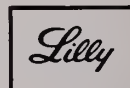
Administration and Dosage: Usual dosage range, 125 mg. (200,000 units) three times a day to 500 mg. (800,000 units) every four hours. For infants, 50 mg. per Kg. per day divided into three doses.

See package literature for detailed dosage instructions for prophylaxis of streptococcus infections, surgery, gonorrhea, and severe infections.

How Supplied: Tablets V-Cillin K, U.S.P., 125 mg. (200,000 units), 250 mg. (400,000 units), and 500 mg. (800,000 units).

V-Cillin K, Pediatric, for Oral Solution, 125 mg. (200,000 units) and 250 mg. (400,000 units) per 5 cc. of solution (approximately one teaspoonful). [042567]

Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana 46206.





Editorials

Perspectives in Medicine*

IN A RECENT TALK on the problems of metropolitan planning, a strong plea was made by the speaker in support of a metropolitan commission then being laboriously debated in the State Legislature. The speaker stated that if every citizen of the Twin Cities could take a trip over the area in a helicopter, particularly at night, there would be complete unanimity of opinion regarding the pressing need of a potent Metropolitan Commission. One would immediately appreciate the absurdity and artificiality of boundaries between our various communities, municipalities and villages in relation to the whole.

Similarly, in this era of rapidly changing social and scientific concepts, our profession urgently needs means of gaining the broadest possible perspective of medicine, historically, socially, scientifically, and practically, so that we can appreciate and recognize real values and preserve them for the future. Also, we must learn to recognize artifacts, sort them out and find ways to discard them.

For all but a century of the 3000 years for which there is a record of medicine, the physician had little to offer his patient in a

modern, scientific, curative sense. His continued high regard by society was derived from his dedication to duty, compassion, empathy** and devotion to his patient, qualities that you no doubt are still taught informally and by example in our schools but are hardly subjects for inclusion on your examinations. In our generation, when for the first time in history we have much to offer our patients in a curative sense, medicine has toppled from its pinnacle of public acclaim. During the many years when the physician employed his art in caring for his patient, the public forgave him his shortcomings, did not expect perfection of him and allowed him to maintain his independence. Indeed, it was essential that he remain independent when he practiced in a highly individual fashion, as this close interpersonal attachment to his patient was an essential ingredient of the practice of his art. But it was his devotion to his patient, his sincere efforts to help and comfort a sick fellow man that society has always recognized, respected and honored. Certainly in a physical sense there is hardly anything noble about incising an abscess or producing an avenue to drain accumulated, decaying body excreta, other than that they are done to relieve suffering or save the life of another human creature.

*From a talk given to the graduating Senior Class of the University of Minnesota Medical School at the annual Minnesota Alumni and medical student dinner, April 26, 1967.

**See Test Your Word Score Page 1823.

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Indications: Hypothyroid conditions. **Contraindications:** Thyrotoxicosis, acute myocardial infarctions unless associated with hypothyroidism. In hypothyroidism with hypoadrenalism coadministration of corticoids with LETTER[®] is recommended. **Precautions and Side Effects:** Excessive dosage may result in diarrhea, cramps, palpitation, nervousness, rapid pulse, sweating. If symptoms appear, discontinue medication for several days, then reinstitute at a lower level. Since myxedema patients with heart disease may suffer seriously from abrupt increases in dosage, caution should be exercised in adjusting dosage. **Dosage:** Generally, the initial adult dosage is 0.1 mg. daily. This may be increased in small increments every one to three weeks until proper metabolic balance is achieved. **Available:** Bottles of 100 tablets, in six potencies: 0.025 mg. (violet), 0.05 mg. (peach), 0.1 mg. (pink), 0.2 mg. (green), 0.3 mg. (yellow), and 0.5 mg. (white).



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It is devotion to the service of mankind, be it in medicine, politics or religion, that has always gained the respect and admiration of society. This is a highly personal act, one that you cannot legislate, unionize, socialize or regiment. In our modern era, the addition of science to the art of medicine has brought many unforeseen benefits to mankind. Although the list of diseases that now can be considered curable is far beyond the imagination of the most visionary physician of a generation ago, we will continue to struggle with unsolved problems that are many times greater and more numerous than those that have been brought under control. In a sense, we all are and always will be on a sinking ship. The only variant is time. Such being the case, in spite of our much publicized successes, we have no basis for assuming any pose of perfection. Nevertheless, because of injudicious publicity and notoriety brought about by occasional publicity-conscious members of our profession and news media ever ready to feed the voracious and sensational appetites of a health-conscious public, perfection is what the public has come to expect of us. We have allowed our success to be overpublicized, we have permitted the press to promise cures in

the offing which we cannot produce and we have had created for us an atmosphere and belief that science will conquer all. The facts of the matter are that this type of glamour has tended to erode the art of medicine, and as a result, to depersonalize medicine. As this trend continues, the human qualities of medicine are submerged and lost; it ceases to be an art and becomes a highly skilled craft. Crafts, but not arts, are unionized, standardized and socialized.

If we lose our dedication to the dignity of man in the practice of medicine, we lose also the moral force that gives it substance. When we subtract this quality from medicine, it becomes a branch of zoology with an exaggerated preoccupation and concern for a single animal species. In your busy days ahead, remember to practice your art. Do this not as a set of slick bedside manners to substitute for competence, or as a bag of tricks for considered rational thought, but do it in the sense that you bring sincerity, skill, devotion and kindness to your patient. Walk humbly with your fellow man, for you will have great need to do so.

Arnold J. Kremen, M.D.
Minneapolis, Minnesota

Niacin: Another New Cure for Schizophrenia?

THERE ARE TWO current biochemical lines of investigation to the study of schizophrenic illness.³ Abnormalities in plasma proteins, for example, have been postulated, but results so far seem essentially inconclusive and unspecific, and may be related to the effects of chronic institutionalization. Disturbances in amine metabolism have also attracted considerable attention with abnormal derivatives of epinephrine being implicated.⁵ Adrenolutin, for one, certainly produces changes in perception. With this metabolite hypothesis in mind, Hoffer and Osmond¹ have used massive doses of niacin (or its relative nicotinamide) as methyl acceptors, for competitive blockade. Because the toxicity of this vitamin (B-3) is extremely low, their regimen of three or more grams per day has induced few side effects.

Vitamin C and penicillamine (Cuprimine) have supplemented niacin in certain cases in their hands. They report good results, but there has been little confirmation and little enthusiasm for their vitamin therapy in schizophrenia. With nicotinamide being an integral constituent of nicotinamide adenine dinucleotide, also called Coenzyme 1, or DPN, Hoffer and Osmond² turned to employing this substance, advanced striking claims for its quick effectiveness, and suggested that schizophrenia is a nicotinamide adenine dinucleotide-deficiency disease. The first published reports from other research facilities on nicotinamide adenine dinucleotide (by Kline et al.⁴ for example) have produced definitely negative findings. Much research is in progress, but judgment must be suspended about niacin and nicotina-

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. A brief precautionary statement follows.

Contraindications: Glaucoma, prostatic hypertrophy, stenosing peptic ulcer, pyloroduodenal obstruction, or bladder neck obstruction.

Precautions: Use cautiously in the presence of hypertension, hyperthyroidism, coronary artery disease; warn vehicle or machine operators of possible drowsiness.

Usage in Pregnancy: Use cautiously, especially in the first trimester. **Note:** The iodine in isopropamide iodide may alter PBI test results and will suppress ^{131}I uptake; discontinue 'Ornade' one week before these tests.

Adverse Reactions: Drowsiness; excessive dryness of nose, throat or mouth; nervousness; insomnia. Other known possible side effects of the individual ingredients: nausea, vomiting, diarrhea, rash, dizziness, fatigue, tightness of chest, abdominal pain, irritability, tachycardia, headache, difficulty in urination. Thrombocytopenia, leukopenia and convulsions have been reported but no causal relationship has been established.

a stuffy nose
is no
laughing matter

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mide adenine dinucleotide until much more evidence is available. In the biological treatment of the group of symptoms called schizo-

phrenia the more customary use of convulsive therapies and antipsychotic agents like the phenothiazines is for now the more desirable approach.

Murray S. Locke, M.D.*
Minneapolis, Minnesota

*Minneapolis Clinic of Psychiatry and Neurology.

References

1. Hoffer, A., and Osmond, H.: *How to Live with Schizophrenia*. University Books, New Hyde Park, New York, 1966.
2. Hoffer, A., and Osmond, H.: Nicotinamide Adenine Dinucleotide (NAD) as a Treatment for Schizophrenia. *J Psychop* 1:3, 1966.
3. Kety, S. S.: Current Biochemical Approaches to Schizophrenia. *New Engl J Med* 276:325, 1967.
4. Kline, N. S., Barclay, G. L., Esser, A. H., Cole, J. O., Lehmann, H. E., and Wittenborn, J. R.: Diphosphopyridine Nucleotide in the Treatment of Schizophrenia, *JAMA* 200:881, 1967.
5. Osmond, H., and Hoffer, A.: A Comprehensive Theory of Schizophrenia. *Int J Neuropsychiat* 2:302, 1966.

Adenoidectomy for Secretory Otitis Media

DR. DONALDSON* has presented the indications for tonsillectomy and adenoidectomy in a logical fashion which should be helpful to physicians actively engaged in the care of children.

Secretory otitis media resulting from adenoids obstructing the pharyngeal orifice of the eustachian tube is a common problem and should be dealt with aggressively. There are three good reasons for this statement. First, these ears are often very susceptible to recurrent acute suppurative otitis media and its complications; second, a child in preschool educational activities or in school with a 30 to 40

db bilateral conductive loss of hearing resulting from sterile fluid in the cavities of the middle ear is handicapped; and, third, long-standing secretory otitis media as an etiologic factor in the formation of an epitympanic cholesteatoma (primary acquired cholesteatoma) has been recognized and continually emphasized since 1890.¹

When adenoidectomy is performed for secretory otitis media it must be done under direct vision for thorough removal, with utmost care not to injure the opening of the eustachian tubes and in association with myringotomy, preferably with the aid of a dissecting microscope.

D. Thane Cody, M.D., Ph.D.
Rochester, Minnesota

*Donaldson, J. A.: The Tonsil and Adenoid Problem. *Minnesota Med* 50:933, 1967.

Reference

1. Bezold, F.: Cholesteatom, Perforation der Membrana Flaccida Shrapnelli und Tubenverschluss: Eine ätiologische Studie. *Z Ohren* 20:5, 1890.

Continuing Study of Chemotherapy for Tumors of the Head and Neck

THE ARTICLE on the use of chemotherapeutic agents used to obtain better control of malignant lesions of the head and neck* covers the subject well in general. The complications and difficulties posed by the use of such drugs

and the techniques employed should be reemphasized. Because of the problems related to the use of chemotherapeutic agents and the techniques required for their administration, team efforts at a specialized treatment center are essential. This point also bears reemphasis. The difficulties in forming cooperative

*Daly, J. F.: Chemotherapy in the Treatment of Head and Neck Cancer. *Minnesota Med* 50:1016, 1967.



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nonfatiguing flavor/smooth pleasant texture; both assure patient cooperation during long-term therapy.

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and well-controlled studies are noted and will continue to present problems in comparative data.

Unfortunately, an awareness of the character and complications of drug therapy and the establishment of improved means of administration have not been accompanied by the rapid development of more effective chemotherapeutic agents. For the present, therefore, workers who direct their efforts toward

improving the results of treatment of malignant disease must utilize currently available drugs and techniques. These efforts will involve continued attempts at earlier detection and additional trials with dosage schedules and timing of chemotherapy. The use of an individual drug and combinations of drugs in conjunction with surgical treatment and irradiation will be a necessary part of these efforts.

Richard G. Hahn, M.D.
Rochester, Minnesota

Tendon Injuries*

THE LACERATED finger tendon generally heals without difficulty; for it to glide is another matter. Tendons heal by proliferation of surrounding tissue, either paratenon or sheath. Evidence that there is any intrinsic tenoblastic activity is lacking. Proliferation of fibroblasts in the peritendinous tissue is evident by the fourth post-injury day and is continuous for about three weeks. If by chance or operative intervention the tendon ends are in approximation, bridging and eventually firm anastomosis occurs. Unfortunately, proliferative activity is as unselective as it is exuberant, and adhesions are the rule. Hopefully, in time these adhesions will stretch and permit useful motion. Obtaining a gliding tendon anastomosis depends on many factors: location of tendon laceration, degree of initial trauma, type of treatment (anastomosis or tendon graft), timing of the definitive procedure, mechanics of surgical technique, presence of infection and the character of the after-care. Many would justifiably add to this list the factor of luck.

Innumerable agents have been laced around tendons to prevent adhesions from forming while the tendon ends are uniting. The following materials have been tried, either clinically or experimentally: nylon, cellophane, teflon, polyethylene, millipore, ivalon, silastic, stain-

less steel and vitallium. Following placement of synthetic blocking tubes, granulation tissue formed by peritendinous tissue must grow beneath the edges of the tube at both ends and advance slowly along the surface of the tendon. Only when this proliferating tissue reaches the anastomosis site does any healing occur. Unfortunately, thick, vascular, limiting adhesions form at either end of the tube. These adhesions never become filmy and mobile. Since nutrition is compromised by the tube itself, various degrees of avascular necrosis and karyolysis** of the tendon occur. This is especially a problem when a free tendon graft is used.

Somehow the effects of the eventual and inevitable tendon adhesions must be minimized. It has been shown repeatedly that adhesions occur only at suture sites and at points where the integrity of the tendon surface is broken. An uncompromised and untraumatized glistening tendon surface will not adhere to surrounding tissue. The task is therefore to handle the tendon with exquisite care, to breach the integrity of its surface only at suture sites and with only the most non-reactive materials. By following the basic principles of tendon repair with continual emphasis on gentle atraumatic technique one can expect the inevitable adhesions to be few in number and ultimately filmy and loose.

Capt. Michael W. Davis
98th General Hospital
A.P.O. New York, N.Y.

*Peterson, Hamlet A. and Lipscomb, Paul R.: Lacerations of Hand Tendons—Current Concepts of Treatment. Minnesota Med 50:101, 1967.

**See Test Your Word Score Page 1823.

He can't sit on two stools with only one rump.—David Dubinsky

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Management of Acute Suppurative Sinus Disease

DR. HILL'S* TITLE specifies suppurative sinus disease. This is particularly important in view of the widespread advertising of medications for "sinus miseries" appearing in television, radio, and the press. One of the primary requirements for treatment of sinusitis is diagnosis, and the primary requirement for diagnosis is to differentiate actual disease of the sinuses, whether suppurative or allergic, from the myriad complaints of "sinus" which come to the attention of the physician. These complaints are based on various headaches, fatigue, stuffy nose, dryness in the nose from poor humidification, mucus in the throat, and various neuroses and inadequacies. Differentiation is important because, as stated by Dr. Hill, suppurative disease of the sinuses responds favorably to treatment. Allergic disease responds less favorably. The various symptoms that the

patient attributes to the sinuses as a result of exposure to advertising claims cannot be expected to respond to treatment for an infection or an allergy. Considerable effort on the part of the physician in taking an accurate history and, in many instances, physical examination or laboratory examinations or both are necessary to differentiate the causes of these various symptoms, so that effective treatment may be applied. In many instances, reassurance and an explanation of the nature of the nose and its function is all that is required. In others, treatment for headache or for nervousness may be in order if the patient is to be relieved. It is unfortunate that the advertising of over-the-counter drugs is not under the same stringent control as advertising of prescription products; much misunderstanding and apprehension might thus be avoided.

Kinsey M. Simonton, M.D.
Rochester, Minnesota

*Hill, F. T.: Management of Acute Suppurative Sinus Disease. Minnesota Med. 50:867, 1967.

Test Your Word Score

Pneumoconiosis—*a chronic fibrous reaction in the lungs to the inhalation of dust* (page 1787).

Necrobiotic—*characterized by partial death of the cells* (page 1789).

Jacksonian—*characterized by involuntary clonic movements with retention of consciousness* (page 1797).

Ketogenic—*producing acetone* (page 1798).

Avicenna—*Arab physician (980-1037)* (page 1799).

Paramount—*superior to all others* (page 1805).

Empathy—*the capacity for participating in another's feelings* (page 1815).

Karyolysis—*dissolution of the nucleus with loss of its affinity for basic stains* (page 1821).

Dharma—*social function—conformity to one's duty and nature* (page 1829).

Turkish proverb—*"He who would desire change had better have one foot in the stirrup."* (page 1829).

Paresthesias—*Abnormal sensations arising spontaneously, distinguished from dysesthesias which are abnormal sensations arising only after cutaneous stimulation* (page 1841).

Anacrotic—*characterized by a small additional wave or notch in the ascending limb of the pulse tracing* (page 1870).

Leukonychia—*a whitish discoloration of the nails* (page 1877).

Pancytosis—*abnormal increase in all the cellular elements of the blood* (page 1881).

Agnogenic—*of unknown cause* (page 1881).

Remanded—*sent back* (page 1919).

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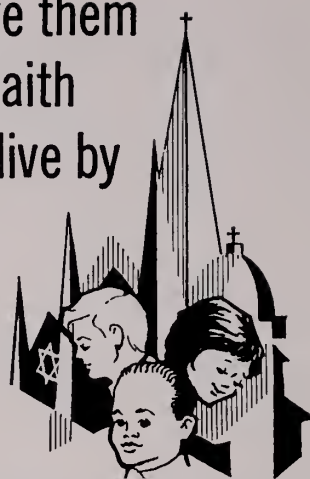
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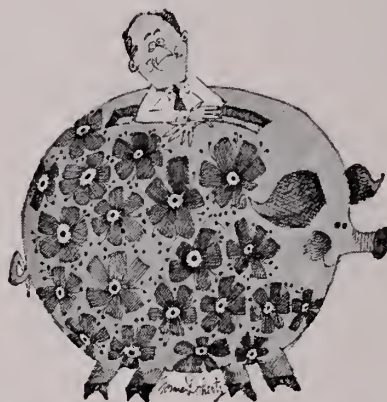
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THIS SPACE CONTRIBUTED BY THE PUBLISHER.

You May Be Right

Your Stature

In your Soliloquy, *For Whom Does the Bell Toll*, in the July issue of MINNESOTA MEDICINE you wrote: The dietary inadequacies of three or four generations ago undoubtedly contributed to the smaller stature of our grandparents as compared with the increased stature of the draftees in World War II.

Did you mean to imply that taller stature is *per se* an evolutionary asset to man? I have yet to meet up with a biologist who considers greater human stature as having survival advantage. Aside from running faster and reaching higher, capacities no longer required by man's natural environment, does taller stature correlate with increased economy and efficiency in the human body?

In fact, may not greater stature be regarded as a biological over-specialization that could run *Homo sapiens* into an evolutionary dead end and possible extinction? Witness the dinosaurs who succumbed to overspecialization: a prime example of a species that became extinct when its food supply failed to remain commensurate with its size.—E.G.R.

EDITOR'S NOTE: Under ideal circumstances—vitamins, minerals, proteins and a host of other things, from birth through the growing period, presuming also that the endocrine balance within the body was also ideal—I expect a species would attain a rather fixed stature in accordance with their basic genes. It might get rather involved, though, if one were to amalgamate the black, white, yellow, and brown races.

In the human with 22 genes and presuming 1000 characteristics to produce a perfect giant, the possibility of another would be $\frac{1}{2}$ of 22 to the thirteenth power. That's in the trillions.

Work and Fatigue

Thanks so much for the Editor's Soliloquy pertaining to work and rest. You hit the nail squarely on the head with every sentence.

Soon after the philosophy of less work and more rest was getting under way a few decades ago, I prepared a manuscript entitled "Work and Fatigue." I am sure that honest labor from the time of John Smith in Colonial days to the present (1929), will continue to be the main cause of prosperity among people everywhere in the world.

J. A. Meyers, M.D.

EDITOR'S NOTE: I wish to quote from that manuscript, in effect:

"To prescribe discontinuance of work and a long period of bed rest for one who has previously been healthy is worse than the most bitter medicine. Unfortunately the idea is extant that work is harmful; that it jeopardizes health. This perhaps is partially responsible for a great deal of dissatisfaction and has led to unreasonable demands for reduced working hours. 'An idle brain is the Devil's work shop' applies as well as to an idle body. To labor to the point of fatigue is not harmful to the healthy body and mind; in fact, it in-

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duces better relaxation and sleep. But the person who spends six hours in ordinary work and devotes the remainder of the day to idleness or worthless recreation is loyal neither to his nation nor to his mind and body.

"At present [1929] there is a good deal of complaint about 'hard times.' I am convinced that much of the difficulty is due to the fact that many are not devoting themselves to their work as diligently as they should, nor as assiduously as they did a decade or more ago.

"I do not recall ever having seen a healthy person harmed by work, but I have seen many who have blamed their work for their illnesses. The Creator very wisely protected us from overwork by endowing us with a sense of fatigue, which usually impels us to discontinue labor before we overexert our muscles to the point of harm.

*"We continually see people who, at the age of thirty-five or forty, appear older than others at the age of sixty or seventy. They are badly stooped and their mentality has deteriorated; they do not remember well; they do not converse as freely as they did in the past; they do not enjoy reading; in fact, life has become more or less a bore and a burden to them. They have allowed their mind and muscles to become flabby and useless because of inactivity."**

Jay A. Meyers has no doubt been a stimulus to more men than he realizes, currently.

*The Trained Nurse and Hospital Review, May, 1929.

Army of Friends

Blood donors are treated with great concern in the Soviet Union. Their health and living conditions are thoroughly investigated. Donorship is honored. The outstanding social service of those who give their blood to the sick, is rewarded with "Honored Donor" badges.

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Blood transfusion is organized on a great scale. Even pre-war figures speak of this. There were 2,433 blood transfusions in 1932, 22,160 in 1935, and 100,143 in 1938, while in 1940 their total jumped to 226,000.

Wide use of conserved blood was first made in 1934, when 4,429 of the total 12,942 transfusions, or 26 per cent, were made with conserved blood. In 1938 this figure climbed to 70 per cent, and in 1940 to 90 per cent.

In the Soviet Union scientists and entire institutions carry on their work under exceptionally favorable conditions. Like all public health facilities, blood transfusion has always been a matter of state concern.

The Moscow Institute of Hematology and Blood Transfusion, the first of its kind in history, was founded in 1926. In its wake similar institutes were established in almost all the major Soviet cities—Kharkov, Leningrad, Tbilisi, Minsk, and others.

In 1941, the U.S.S.R. had about 1,500 institutions specializing in blood transfusion. Today every single point in the Soviet Union, including the Far North, has transfusion facilities.

Like all other forms of medical treatment, even the most complicated blood transfusions are made free of charge. Their cost is covered by the state budget.*

*L. Fridland, M.D.: The Achievement of Soviet Medicine, 1961, edited and translated from the Russian by W. Horsley Gantt, M.D.

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Robert W. Goltz, M.D., Denver, Colo.—*Dermatology*
Charles H. Brown, M.D., Cleveland, Ohio—*Gastroenterology*
George E. Burket, Jr., M.D., Kingman, Kan.—*General Practice*
J. George Moore, M.D., New York, N. Y.—*Gynecology*
William Damashek, M.D., New York, N. Y.—*Internal Medicine*
Oglesby Paul, M.D., Chicago, Ill.—*Internal Medicine*
John A. Aita, M.D., Omaha, Neb.—*Neurology*

Robert B. Wilson, M.D., Rochester, Minn.—*Obstetrics*
Mack L. Clayton, M.D., Denver, Colo.—*Orthopedic Surgery*
William H. Saunders, M.D., Columbus, Ohio—*Otorhinolaryngology*
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Pre-Assembly Special Symposium—Sunday, March 3—"Sexual Problems in Clinical Practice."

The Editor's Soliloquy

Evolution or Revolution?

Two Feet in the Stirrups: Physician or Technician

MANY EXCELLENT technical operators have been produced in experimental laboratories from high school graduates. These technicians have mastered the steps of medical and surgical procedures and know how to perform well at the direction of their mentor. Nurses and others have learned to do accurate laboratory routines and execute the infinitely precise details of an intensive care or cardiac recovery room in accordance with the directions of a knowledgeable physician.

The majority of technicians know only the rudiments of medical or surgical indications for the procedures they perform so competently and even less about the pathologic processes involved.

The glory of these dedicated employees is unsung in the annals of medical history. They simply work a 40-hour week, collect their bi-monthly check and receive their pay raises in accordance with their tenure. Such is the character of the technician.

The physician, like the technician, performs with precision and proficiency. But no follower he! His role is that of initiator, for therein lies his dharma.* The doctor's long and arduous working hours do not fit into a convenient schedule and his monetary reward is no more than commensurate with the value of his service to his community. His capacity for infallible decision and judgment must be tempered to the quality of the finest steel through diligent study and adequate training in the basic sciences, metabolic processes, and their potential pathology. He must be capable of meticulous evaluation of abnormal physiologic signs from hour to hour; he must recognize almost instinctively the surgical risks and the medical alternatives thereto.

He must also be adept in the psychological management of the patient—in and out of balance—both individually and family-wise. These qualities are integral to his makeup—unadorned with splash and splendor and often unidentifiable to the casual observer. Such is the character of the physician.

The categorical distinction between the technician and the physician lies in the extra-dimensionality of the doctor's sphere: in his art which consists of a distillate derived from the twin disciplines: the scientific and the humanistic. Only a study of the liberal arts, requiring time and maturation, can furnish the broader outlook and deeper insight so invaluable and indispensable to a doctor dealing with human nature as well as with diseased bodies.

Change is ubiquitous and perennial; but let us not be under the illusion that change always represents progress. It is that extra-dimensionality that Medicine must not forfeit in a quest for earlier specialization. If we can keep both feet firmly and confidently planted in the stirrups* and be prepared to advance, then it is conceivable that the next 50 years could duplicate the past 50 which have already produced more advances in medicine than all the preceding half-centuries.

Granted, however, that some changes may be desirable, it would seem unnecessary to start a revolution in medical education in order to rectify a few current teaching errors.—Carl O. Rice, M.D.

*See Test Your Word Score Page 1823.

Old Doc Hess Says: I have never known a dying man who believed in euthanasia.—COR



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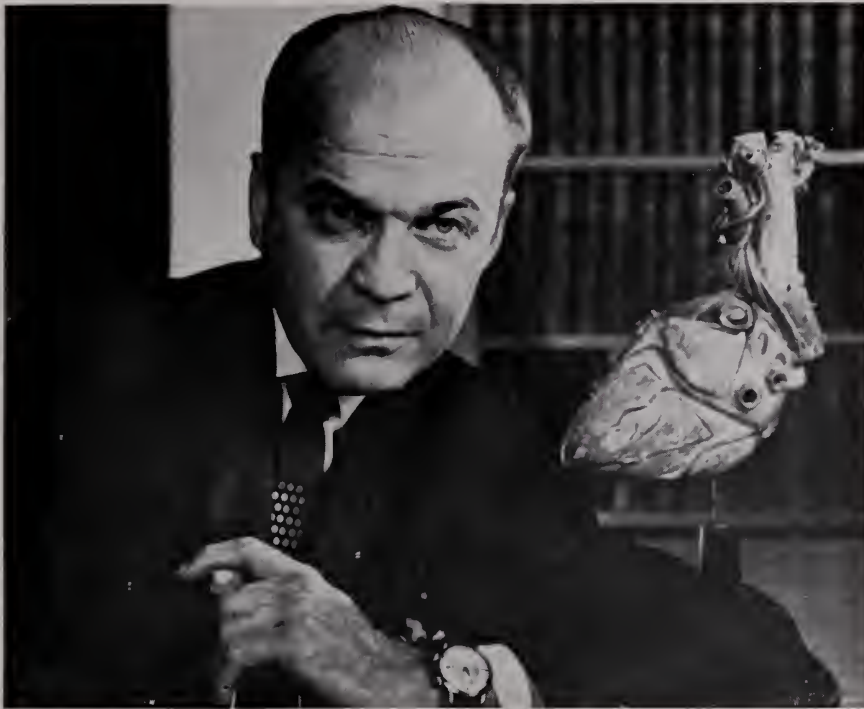
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C. Walton Lillehei, M.D.

On October 7, 1967, Dr. C. Walton Lillehei was honored at a Testimonial Dinner at the Hotel Radisson, Minneapolis, by his present and former fellows in cardiovascular surgery, prior to his assuming the position of Lewis Atterbury Stimson Professor of Surgery and Chairman of the Department of Surgery, Cornell University Medical Center—New York Hospital on November 1st.

The esteem with which Doctor Lillehei has always been held by his former fellows was exemplified by many, such as Dr. Alberto Spoerer (Santiago, Chile) and Dr. Denis Thompson, (Bulawayo, Rhodesia) who traveled great distances for the occasion.

We Extend to Him this Tribute

I am happy to be here with these interesting surgeons. I am proud to have been included on this occasion. I feel humble to sit among you, and as I meditate thinking of you, Walt Lillehei, I wish that I had known more intimately some of your illustrious peers, predecessors though they be.

I wish I had known *Ambroise Pare*, a patient man, the Prince of Surgeons, back in the 16th Century when he reinstated in France the practice of ligaturing instead of cauterizing blood vessels after amputation. If I had been there I would have defended him vigorously against the opposition of his reactionary colleagues. It would have been interesting to see him take exception with the King of France, who was an ardent advocate of the value of the stag stone as an antedote against snake bite, and who then, after suggesting that the King try the experiment on some of his condemned prisoners, found that the experiment failed.

I wish I had known the *industrious William Harvey*, the father of physiology, who, in 1628, announced his revolutionary discovery that the blood circulates, leaving the heart by the arteries and returning by the veins. From

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that historic day on doctors knew that in order to prevent bleeding from the vessels, the arteries had to be ligated toward the heart and the veins away from the heart.

I am sure that I could have enjoyed the *indefatigable meticulous technician, John Hunter*, who in 1785 carried out his bold operation on an aneurysm of the popliteal artery, postulating its effectiveness based on earlier experiments on the antler of a deer, in which he had demonstrated the collateral circulation. I would have enjoyed visiting his menage where he kept a conglomeration of animals, dead and alive, for purposes of observation, examination, experimentation and anatomical dissection.

I should like to have known the *far-sighted Louis Pasteur* and to have joined him in his laboratory during the 1860s, when he looked through the microscope and then carried out experiments to prove that the micro-organisms causing disease were not self-generating, thus leading to the use of carbolic acid as an antiseptic in surgery; this in turn causing the *courageous Joseph Lister* to crusade for antiseptics against the opposition of the non-Listerians who ridiculed him for dousing his patients, spraying the walls, soaking his instruments and hands with disinfectants.

I could have enjoyed knowing the *versatile Swiss surgeon, Theodore Kocher*, who, in the 1880s, made surgery on the thyroid safe, and who in 1909 was the first surgeon to be awarded the Nobel Prize, for his monumental work on goiter.

I wish I had known the *ingenious innovator, Eldorado Bassini* of Padua, in 1888, when he performed one of the first anatomical procedures for the cure of hernia, and after the operation tickled the throat of his patients in order to make them cough and gag to test the strength of his surgical repair.

These men were pioneers, each in his own field; they were ingenious, versatile, courageous, indefatigable, far-sighted, industrious, and patient men. I predict that one of my progeny will some day be reciting a similar list of historical luminaries in the field of surgery much as I have done this evening, boasting pridefully that their great-grandfather knew intimately, shook the hand of, and visited with one of the great pioneers of my time, a man who possessed all of these great qualities and received recognition—the man who made surgery on the heart safe and a common, everyday procedure: C. Walton Lillehei! To you, Walt, a Salute!—Carl O. Rice, M.D.

False Trails and Byways

The healing art was bound to fall into errors. It could not avoid them, for the remedies at its disposal were inadequate for the tasks it was set. The tasks were not shelved—but discharged by makeshift solutions which became sanctioned errors.

But that is the way of science: "We must exhaust the error—and often the idiocy—before we can work our way towards the beautiful goal of calm wisdom."

—Schiller

Temperature

Very high and very low temperature extinguishes all human sympathy and relations. It is impossible to feel affection beyond 78 degrees, or below 20 degrees of Fahrenheit; human nature is too solid or too liquid beyond these limits.

—Sydney Smith

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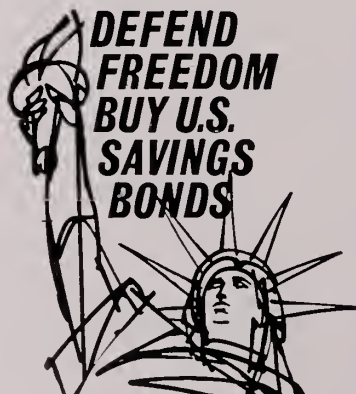
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QUESTION: One of my patients, a 56-year-old man with Laennec's cirrhosis, was admitted to the hospital with jaundice, ascites and the characteristic clinical and laboratory findings of advanced hepatic cirrhosis. He improved on a regimen of diet and the circumspect use of diuretics. Today, after two weeks of steady improvement of clinical and laboratory parameters he suddenly developed high fever. There is no sign of urinary tract, pulmonary or central nervous system infection. There was no change in therapy and no manipulation which could have provoked this new event. What might be the nature of this new episode?

ANSWER: It is not unusual for patients with advanced cirrhosis to develop seemingly spontaneous bacteremia. Usually this is a gram-negative bacteremia and its occurrence in cirrhotics is explained as follows: Intestinal bacteria escape from the bowel in normal individuals by way of the venous and lymph channels, but they are effectively intercepted by the reticuloendothelial system of the liver. In the cirrhotic patient, however, the liver can be circumvented by way of the collateral circulation, thus presenting a ready and ever-present threat of gram-negative bacteremia.

We have to assume that this happened to your patient. After you have obtained aerobic and anaerobic blood cultures, you should lose no time in treating this presumed gram-negative bacteremia with a drug, which should cover most or all of the enteric organisms. At the present time a combination of Kanamycin and Cephalothyn would serve this purpose, until blood cultures have established the precise nature of the bacteremia and thus permit more specific therapy. At the first sign of hypotension appropriate measures should be met for the control of endotoxin shock.

H. H. Zinneman, M.D.
Minneapolis, Minnesota

What's on your mind—if you'll forgive the overstatement.

—Fred Allen

Genealogy

Genealogy: an account of one's descent from an ancestor who did not particularly care to trace his own.—Ambrose Bierce

Homeopathy

The vulgar quackeries drop off, atrophied, one after another. Homeopathy has long been encysted, and is carried on the body medical as quietly as an old wen.

—Oliver Wendell Holmes

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The Viewing Box

Shoulder Mass in an Infant

Clinical History

THIS INDIAN female infant was first seen at the age of six weeks because her mother had noted that she suddenly was not moving her right arm. There was no other significant history. Initial examination of the patient disclosed irritability, a fever of 102° , and a large, firm, tender mass over the right shoulder posteriorly to include the axilla. She refused to allow the examiner to move her right arm and moved it herself very little.

Pertinent laboratory data included a leukocytosis of 17,000 with a normal differential, a sedimentation rate of 113 (mm/hr.), and an alkaline phosphatase of 70 (King-Armstrong units).

An electromyogram performed early in the hospital stay showed findings consistent with a right brachial nerve palsy.

What is your diagnosis? (See next page.)



Fig. 1—The initial chest film (7/24/67) discloses a soft tissue mass in the right shoulder. There is an appearance suggestive of early subperiosteal resorption of bone (arrow) on the axillary border of the scapula just below the glenoid. Of no consequence is a healing left clavicular fracture which was traumatic in origin.

Diagnosis: Infantile cortical hyperostosis (Caffey's Disease).

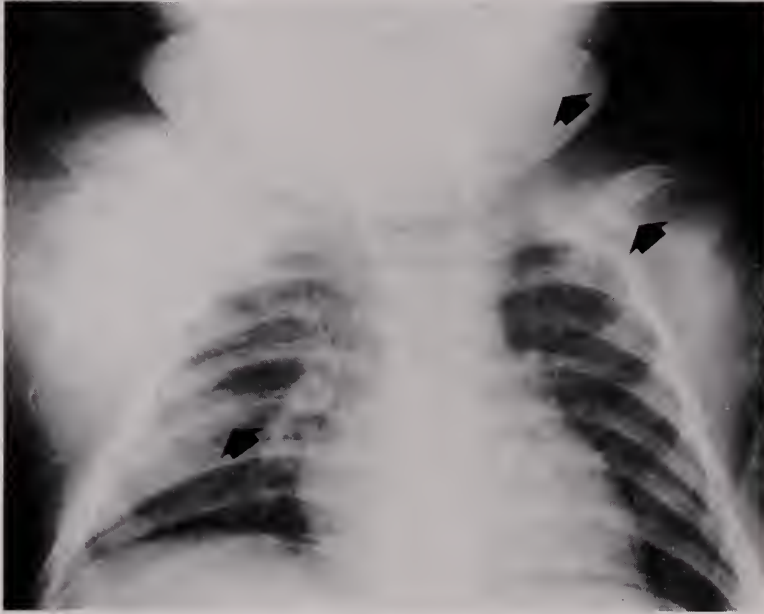


Fig. 2—A subsequent chest film (8/22/67) shows a markedly hyperostotic right scapula which has practically lost its original anatomic form. Note the new born formation (arrows) in the mandible, clavicles, right ribs and the opposite scapula.



Fig. 3—The last film (10/18/67) now shows a marked thickening of the clavicle and several of the ribs. The scapula is still deformed, but there has been considerable resorption of the hyperostoses.

This benign condition, first reported by Caffey and Silverman in 1945, may affect much of the skeleton and its adjacent fascia and muscles. There is no sexual or racial predilection. The average age of onset is nine weeks, no cases reported having begun after nine months of life. Almost all of the patients will commonly have hyperirritability, fever, swelling of the soft tissues and polyostatic involvement with cortical new bone formation.

Changes have been reported in most bones other than the phalanges and vertebrae. Most commonly affected are the mandible, clavicles and ulnae. If confined to only one bone other than the mandible, the picture should be considered due to trauma unless proved otherwise.

The early finding suggesting sub-periosteal resorption of bone in the scapula is of particular interest in this case. Caffey¹ states that this has not been previously observed. When seen in its early stages, Caffey's disease unilaterally involving the scapula (which is usually the case) can be confused with osteosarcoma.

The electromyogram findings suggesting a brachial nerve palsy are uncommon. This could be the result of axillary inflammation and mass effect. The electromyogram reverted to normal when the patient improved clinically.

Although the clinical history and roentgenograms are usually characteristic for this entity, one might include scurvy, rickets, osteomyelitis and trauma in the differential diagnosis.

The disease is usually self-limiting with clinical and radiographic findings reverting to normal within a period of several months. Steroids have been used in the treatment of the disease with success, as in this case. Caffey places all of his patients on a course of steroids.

Charles C. Nicolette, M.D.*

Peter K. Ullrich, M.D.**

Minneapolis, Minnesota

*Fellow, Department of Radiology, University of Minnesota Hospitals and Hennepin County General Hospital.

**Resident, Department of Radiology, Veterans Administration Hospital and Hennepin County General Hospital.

References

1. Caffey, J.: *Pediatric X-Ray Diagnosis*, Ed 5, Chicago: Year Book Medical Publishers, Inc., pp. 961-973, 1967.
2. Gwinn, J. L., et al.: Radiology Case of the Month. Infantile Cortical Hyperostosis (Caffey's Disease), *Amer J Dis Child* 113:471, 1967.
3. Marquis, J. R.: Infantile Cortical Hyperostosis, *Radiology* 89:282, 1967.
4. MacLeod, W. et al.: Infantile Cortical Hyperostosis, *Clin Radiol* 16:269, 1965.

Medical Men on Postage Stamps

Walter Reed (1851-1902), American army surgeon, sanitarian and bacteriologist, who during the Spanish-American war was sent to investigate a typhoid epidemic among the U. S. troops and who in 1900 headed a commission to Havana to investigate its etiology, was honored for his achievements by a commemorative postage stamp issued by the U. S. in 1940. Reed also did valuable research work on cholera and erysipelas, but his main contribution to medicine was his theory that yellow fever was transmitted by a mosquito.

Julius Wagner-Jauregg (1857-1940), Austrian neurologist and psychiatrist, whose malarial inoculation treatment of paresis was 30% successful in a disease previously fatal, and who also made valuable contributions in the fields of cretinism and other thyroid diseases, was honored by an Austrian postage stamp issued in 1957.

Laboratory Diagnosis of Rubella

The Division of Medical Laboratories of the Minnesota Department of Health is now ready to provide serologic tests for rubella. Acceptance of blood specimens for rubella antibody determinations will be limited to the following situations:

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3. Investigation of presumptive complications of rubella (encephalitis, etc.), especially in young children. For this purpose paired acute and convalescent whole clotted blood specimens are required. Specimens from adult males or from children other than those who can qualify in group 3, must be declined at the present time.

Containers for the submission of whole clotted blood are the same as those currently in use for submitting specimens for virus antibody studies. Additional containers are available on request from: Minnesota Department of Health, Division of Medical Laboratories, University Campus, Minneapolis, Minnesota 55440.

It is important to all concerned that specimens be accompanied by completed data cards identifying the patient, giving clinical diagnosis, date of onset of illness, etc.

Minnesota Department of Health
Division of Medical Laboratories

Anesthesia Through Will Power

The use of the will to ease pain must have seemed to verge on the miraculous to those who could not possibly know that we can condition our reactions and responses to a painful stimulus.

Something like this had been demonstrated by the seventeenth century French mathematician, Blaise Pascal. Suffering intense pain from a facial neuralgia, he found himself unable to sleep. Tossing in his agony, he remembered that Seneca, the stoic philosopher of Rome, had once commented: "The more the attention is fixed on the cause which produces pain, the more its intensity is increased; the more a man stands away from it, the more relief he gets."

In desperation, Pascal decided to test this and began to concentrate on a problem in geometry that had puzzled scholars for years. In the course of his intense preoccupation he forgot his pain and solved the problem in one night.

Later, when he was asked to what use he would put his mathematical discovery, he replied: "None. But it was a good cure for a bad night."*

*Bernard Seeman: Man Against Pain.



Neurological Conference

Paresthesias* in an Elderly Patient

Medical History

Doctor Ordean Torstenson**:

This 69-year-old man was first seen in our New Medicine Clinic on December 7, 1966, with a chief complaint of a burning feeling within his mouth and in his left leg, which had first appeared in January, 1965, following a hospitalization for pneumonia. The possibility of an allergic condition was considered at that time, but an allergy evaluation was negative. This discomfort has persisted with the same intensity for the past two years. Occasional mouth washes have relieved the burning in his mouth somewhat for short periods. The burning sensation in his left leg originally was present only in the anterior left hip but subsequently spread to involve his entire left leg. He obtains slight relief of his leg discomfort when walking.

The patient stated that during the past two years he has had numerous hospitalizations at St. Luke's Hospital and Miller Hospital for these complaints; but no attempted treatment has afforded any significant relief. Presently he is taking no medications except for one Contac pill daily for sinus drainage, and Maalox for a peptic ulcer condition which he has had for two and one-half years. Other complaints include shortness of breath on exertion and occasional sharp chest pain when breathing deeply. An increased urinary frequency also bothers the patient at times.

Physical Examination

Physical examination revealed an elderly man with a slightly protuberant abdomen. Although he appeared to be somewhat anxious, he was in no actual distress. His blood pressure was 160/100 mm.Hg. and his pulse 90 per minute. In his mouth there were three canker sores and a questionable area of leukoplakia on the lateral aspect of his left upper alveolar ridge. A few dry rales were present in the base of his left lung. Rectal examination revealed non-inflamed external hemorrhoids. The skin over his lower legs was moderately erythematous and shiny, and numerous small varicosities were present.

Neurological Examination

The neurological examination revealed no definite findings. Vibration sensation was somewhat reduced in his lower extremities, and a positive Patrick's sign was present in the left leg. Mentally the patient showed a mild memory deficit and he was totally incapable of subtracting serial sevens from 100.

*See Test Your Word Score Page 1823.

Neurological Conference held January 12, 1967. These conferences are an integral part of the Comprehensive Clinic Program at the University of Minnesota Hospitals.

**Student doctor, University of Minnesota Hospitals.

Laboratory Findings

Laboratory examination revealed a hemoglobin of 15.4 grams% with a normal hemogram. The urinalysis was unremarkable, BUN 21 mg.%, and a glucose tolerance test was within normal limits. In 1959 the patient had had an abnormal EEG characterized by diffuse theta activity. A repeat electroencephalogram in January, 1967, showed similar slowing occurring bilaterally in regular and irregular runs of activity mainly in the anterior regions of the head. An electrocardiogram was suggestive of an anterior septal myocardial infarct. An upper G.I. examination revealed a small hiatus hernia with gastroesophageal reflux, considerable deformity of the pyloroduodenum and a small duodenal diverticulum in the descending portion of the duodenum.

Initial Impression

Dr. Robert W. Soll:*

This patient has had fairly extensive medical care during the past seven years for numerous complaints, none of which had any particularly localizing value. Furthermore, none of the tests which we have done now have contributed any further insight into the cause of his chief complaint, which is a burning sensation in his left leg and his mouth. The patient's slow mentation and mild memory deficit together with a diffusely abnormal electroencephalogram may be the only significant findings that we have. Together these suggest the possibility of a cerebral degenerative process. Although the BUN is slightly elevated, the patient has no other obvious evidence of renal disease. This will have to be investigated further.

Psychological Evaluation

Mr. William Gayton:**

Several tests were administered in order to evaluate intellectual functioning, personality processes and the possibility of brain damage. In regard to intellectual functioning, the patient shows a discrepancy between his verbal and performance abilities; on the Binet Vocabulary he has an M.A. of 14.7, giving him an approximate I.Q. of 95, which is within normal limits; on the Porteus Maze, which is a perceptual motor task, he has a test age of 11 and 1/2 years, reflecting an I.Q. of only 82, which is in the dull-normal range. Such a discrepancy between verbal and performance measures is not inconsistent with his present age since performance type behavior does decline with age. It should be pointed out, however, that this type of discrepancy is also very frequently found in brain-damaged patients. In those tests to evaluate cerebral dysfunctioning the patient shows deficits in short-term memory and visual motor coordination. Although these tests correlate with his age, I.Q., and education, they would probably be more significant if they were found in a younger person with a higher I.Q. and a broader educational background. The personality evaluation as conducted by the Minnesota Multiphasic Personality Inventory suggested a mildly neurotic profile with depression and somatic overconcern. The depression is most likely a response to the physical pain which he has been experiencing over the past few years. He was somewhat rigid and inflexible on this test, tending to resist any psychiatric explanation of his problem. Correspondingly, he would probably be very resistant to any intervention of a psychotherapeutic nature.

In summary, his most marked deficits were in the perceptual motor tasks and tasks requiring short-term memory, deficits which fall into the brain-damaged category if scored according to the norms. If age, past educational history and other tests of I.Q. are considered, however, the significance of these findings is somewhat questionable.

*Neurologist, University of Minnesota Hospitals.

**Clinical psychology trainee, University of Minnesota Hospitals.

Social Service Evaluation

Miss Helen Kretchmer:*

The patient seems to be a meticulous, conservative individual with expectations of himself that he is unable to fulfill. He hasn't been able to work since 1961 and has become conscious of the cost of his medical care and his dwindling savings. He was retired on disability about the time that he developed an ulcer. He had considered going elsewhere for his medical problems, but his family physician persuaded him to come here because it would probably be less expensive for him.

After finishing part of the 8th grade, the patient quit school because he was the oldest of eight children and was needed on the farm. During World War I at age 17 he enlisted and was able to complete part of the 9th grade while in service. The ship on which he was stationed was sunk, but he was rescued. As a result of a service-connected back injury he received a pension of \$80.00 a month. After service he did some drafting but finally began working in a shipping department as an assistant foreman. The patient underwent considerable nervous tension on this job, a factor which may relate to his eventual development of an ulcer. During the past few years he has been helping around the house and doing a little yard work.

Both the patient and his niece convey the impression that he has always been a rather nervous man. She commented on a book written by a psychologist, which made her feel that her uncle was a neurotic. When she mentioned this to the patient, he became very angry with her. She also mentioned that the patient's father had similar symptoms of burning of the mouth and drooling when he was 52 years of age. After being placed on some type of tranquilizer for a couple of months he recovered. Her own father also had had similar symptoms at age 69 and responded to the same treatment. According to his niece, the patient has always been very restless; consequently, it is difficult to distinguish his present troubles from his past problems.

Neurological Evaluation

Dr. Soll:

Although widely separated in location, the paresthesias which the patient feels in his mouth appear to be similar symptomatically to the burning sensation in his left thigh; however, I know of no way to relate them anatomically. Paresthesias do occur in many conditions, such as traumatic peripheral nerve lesions, multiple sclerosis, tabes dorsalis, and pernicious anemia. *Arteriosclerosis* has been known to be associated with paresthesias, probably the result of an ischemia of the peripheral nerves. Supporting the possibility of a diffuse arteriosclerotic involvement is the abnormal electroencephalogram. Although the changes on the electroencephalogram are not necessarily typical of arteriosclerosis, this possibility certainly exists. In addition, various lesions of the spinal cord, brain stem, thalamus and parietal lobe have produced paresthesias. Unfortunately there are no focal findings to help localize the specific cause in this patient's case.

Often the obvious cause may be an irritative pathological process, but in many instances it may be quite inconspicuous. Clinically, paresthesias developing during the course of a neuropathy such as occurs in *alcoholism or vascular insufficiency* often appear initially after the neuropathy has become well-

*Supervisor, Social Service Department, University of Minnesota Hospitals.

established and convalescence is under way. This might also be likened to paresthesias that develop in an extremity after it has "gone to sleep."

Finally, there is the possibility that the patient's symptoms have a *psychogenic* component. I feel that the patient may be over-reacting to his symptoms. He probably also has had some reduction in intellectual functioning as manifested by his inability to subtract serial sevens from 100 or name the recent presidents. During his clinic visits he has had a great tendency to ramble on about his symptoms or problems.

Although the patient's real problem may be the result of vascular disease, the best treatment would be to reduce his nervousness and anxiety with tranquilizing medications. Hopefully his numerous minor complaints would also subside if he were calmer. Rather than telling him that he is on a tranquilizer, we can simply explain that he needs to be on a special medication to reduce the nerve activity which is causing the burning. If symptoms continue to worsen in the continued absence of any good localizing sign, pneumoencephalography and examination of the spinal fluid could be done as a further diagnostic procedure. In degenerative cerebral diseases, evidence of an elevated spinal fluid protein and cerebral atrophy may be elicited.

Patient is Interviewed.

Dr. Soll:

For what reason did you have to quit work?

Patient:

I had ulcers and a spastic nervous system which the doctors told me was probably the result of my stomach trouble. I could have continued working longer, but one day I passed out at work and couldn't speak. On my way to the hospital in an ambulance my speech returned.

Dr. Soll:

Did you have any weakness?

Patient:

No, only my speech was impaired for a while.

Dr. Soll:

What were you doing at the time that the spell occurred?

Patient:

It happened shortly before quitting time in the afternoon. I began feeling weak and sat down. Apparently I passed out, but when I awoke I was just as normal as before. Following this the company told me to retire. Although the union said they would fight it for me, I decided to quit because I thought the same thing might happen again. What I am concerned about now is the burning in my mouth. If you people tell me that I am mentally disabled or something like that, you are wrong. My faculties are just as good now as they were 30 years ago. I was very much amazed about the tests. I may have a nerve condition—I am not saying that I haven't something minor. Naturally my brain doesn't function as it did years ago. I don't have a large education but I think my body and brain work in proportion for my age with an average education. I have no heart condition and my blood pressure is okay. My father had trouble similar to this and got over it in a few months.

Miss Kretchmer:

You do not feel that you should take public assistance, but you have several debts you are worried about.

Patient:

I am paying \$69.00 a month on our house, as well as trying to keep up the car. We owe our doctor \$400, not counting the medicines. If I have to go on another year like this, I'd rather be dead. I lose sleep and so does my wife.

Patient leaves the conference room.

Discussion and Recommendations**Dr. Soll:**

I would like to start the patient on a tranquilizer. This could be supplemented with a mild antidepressant medication and also with a sedative for sleep, if necessary.

Mr. Gayton:

How might the tranquilizer influence the type of depressive behavior which his Minnesota Multiphasic Personality Inventory indicated?

Dr. Soll:

I don't believe it will affect the depression very much, but it may alleviate some of his anxiety and nervousness.

In regard to the episode of unconsciousness which he had in 1961, it is interesting to speculate that he may have had a transient cerebral ischemia at that time. This would help support the possibility of a cerebrovascular condition.

Mr. Gayton:

Subtle psychological changes reflecting brain damage might be revealed by a special battery of psychological tests developed by Dr. Manfred Meier in the Neuropsychology laboratory.

Dr. Soll:

Frequent visits to the neurology clinic also would help to reenforce the medical therapy.

Addendum

The patient has been treated in the above manner and there has been significant improvement in his symptomatology during the past nine months.

Robert W. Soll, M.D.
Chairman,
Adult Community Services

Participating in the conference were: Student Doctor Ordean Torstenson; Miss Helen Kretchmer, Supervisor, Social Service Department; Dr. Robert Soll, Neurologist and Mr. William Gayton, Clinical Psychology Trainee.

Ignorance

To be ignorant of one's ignorance is the malady of the ignorant.

—A. B. Alcott

Judgment

The average man's judgment is so poor, he runs a risk every time he uses it.

—Edgar Watson Howe

Laughter

Laughing is the sensation of feeling good all over and showing it principally in one spot.—Josh Billings

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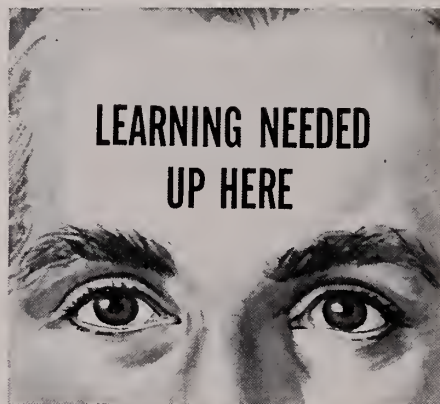
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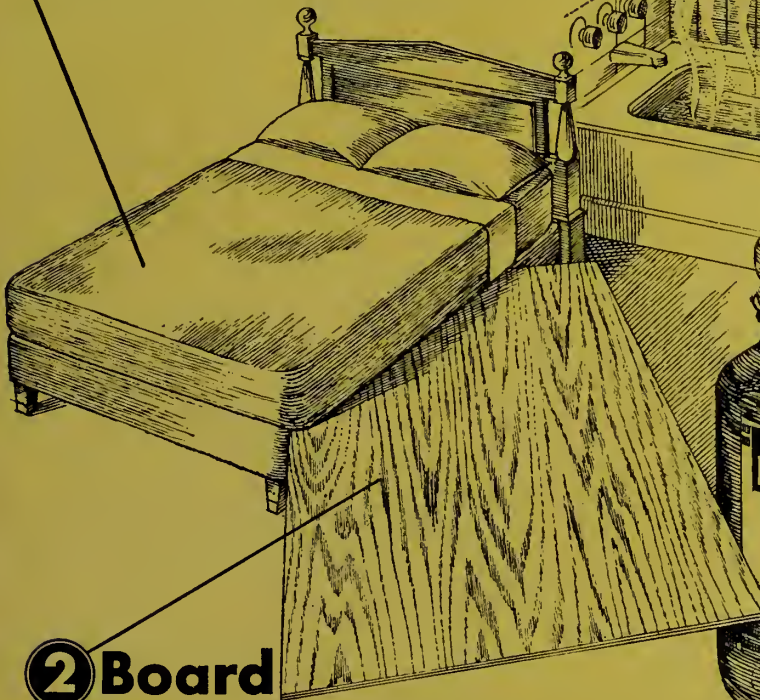
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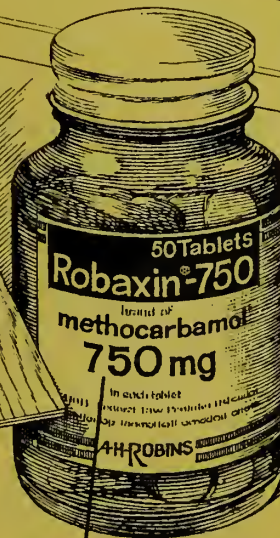
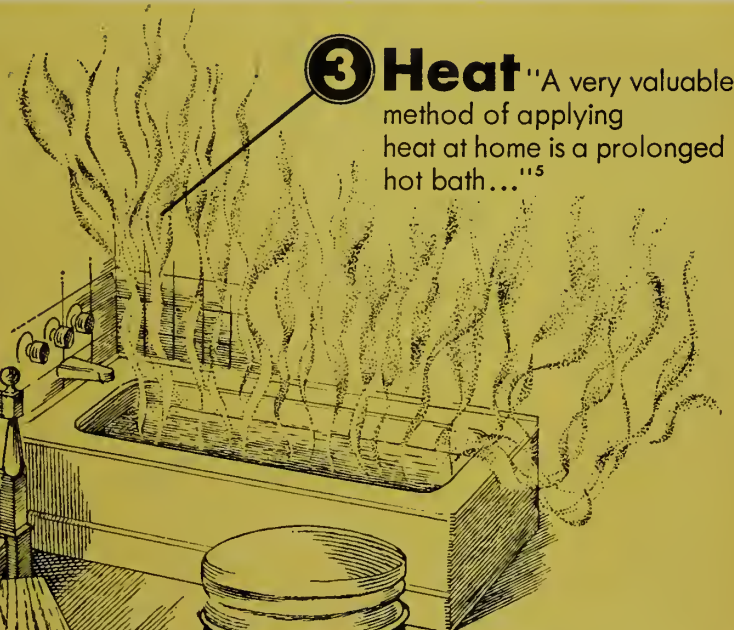
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References: (1) J. Gadsby, C.M.: Applied Therap. 8:950, 1966. (2) J. Gattschalk, L.A.: GP 33:91, 1966. (3) J. Rowe, M.L.: J. Occup. Med. 2:219, 1960. (4) J. Cazen, L.: South Dakota J. Med. 18:26, 1965. (5) J. Sata-Hall, R.: Med. Sc. 14:23, 1963. (6) J. Weiss, M. and Weiss, S.: J. Am. Osteopath. A. 62:142, 1962. (7) J. Feuer, S.G., et al.: New York J. Med. 62:1985, 1962.

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What about switching patients from higher dosage forms?

In transferring patients to low-dose Norinyl-1 from higher-dosage oral contraceptives, some breakthrough bleeding may occur in the early cycles. In the majority of cases the bleeding episode is mild and self-limited. The long-term advantages of the lower dosage form should be weighed against the inconvenience of possible breakthrough bleeding in the individual patient.

Prescribing Information

Contraindications: Patients with any symptoms or history of thrombophlebitis, pulmonary embolism, liver dysfunction or disease, carcinoma of breast or genital organs, or undiagnosed vaginal bleeding.

Warnings: Discontinue medication pending examination if there is sudden partial or complete loss of vision, proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions, medication should be withdrawn. The safety of Norinyl-1 in pregnancy has not been demonstrated. If a patient misses two consecutive periods, pregnancy should be ruled out before continuing the medication. If she has not adhered to the prescribed schedule, pregnancy should be considered at the first missed period. Active ingredients of oral contraceptives have been detected in the milk of mothers who received these drugs; the significance to infants has not been determined.

Precautions: Pretreatment physical should include examination of the breasts and pelvic organs, as well as a Papanicolaou smear. If endocrine or liver function tests are abnormal during therapy, repeat tests are recommended after the drug has been withdrawn for two months. Following administration of drug, preexisting uterine fibromyomata may increase in size. Careful observation and caution are required for patients with symptoms or history of epilepsy, migraine, asthma, cardiac or renal dysfunction, cerebrovascular accident, psychic depression, and diabetes. In cases of undiagnosed vaginal bleeding, adequate diagnostic measures are indicated. Possible long-term effects of the drug on pituitary, ovarian, adrenal, hepatic or uterine function must await further studies. The physician should be alert to the earliest manifestations of thrombophlebitis and pulmonary embolism. The drug should be used judiciously in those young patients in whom bone growth is not complete. The age of the patient constitutes no absolute limiting factor, although treatment with Norinyl-1 may mask symptoms of the climacteric. The pathologist should be advised of Norinyl-1 therapy when relevant specimens are submitted.

Side Effects: The following have been observed with varying incidence in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms, breakthrough bleeding, spotting, change in menstrual flow, amenorrhea, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately postpartum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals, mental depression. Although the following side effects have been reported in users of oral contraceptives, no cause and effect relationship has been established: anovulation posttreatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption, and itching. The following occurrences have been observed in users of oral contraceptives (a cause and effect relationship has neither been established nor disproved): thrombophlebitis, pulmonary embolism, neuroocular lesions.

The following laboratory tests may be altered by the use of oral contraceptives: increased sulfobromophthalein and other hepatic function tests, coagulation tests (increase in prothrombin, factors VII, VIII, IX and X), thyroid function (increase in PBI and butanol extractable protein-bound iodine and decrease in T^3 values), metyrapone test, pregnanediol determination.

norethindrone — an original steroid from
SYNTEX 
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Here's why Norinyl-1 makes medical sense.

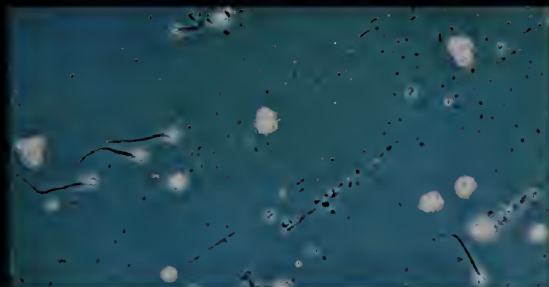
The effectiveness of Norinyl-1 as a low-dose oral contraceptive may be explained by its possible multiple action. In addition to its primary action of suppression of ovulation, Norinyl-1 may offer additional protective mechanisms... (1) creation of a cervical mucus that may be hostile to sperm penetration, and (2) development of an endometrium that may be out of phase with nidation.

These effects are illustrated below.

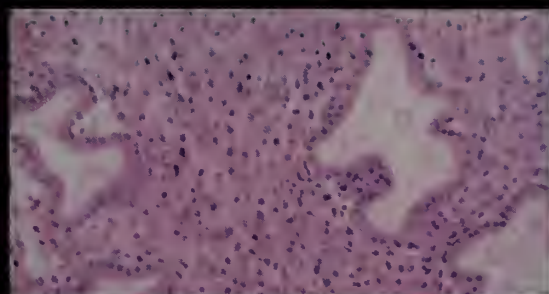
Untreated Patient



Cervical mucus at midcycle is usually thin and watery, with Spinnbarkeit (stretchability) of 15 to 20 cm.



Spermatozoa appear healthy, active, freemoving.

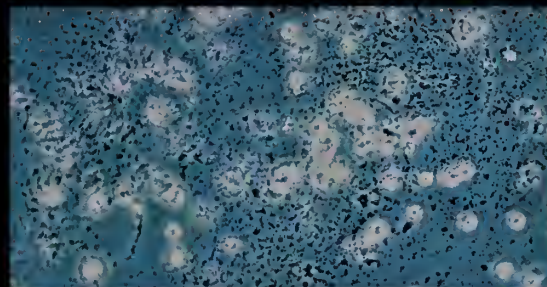


Endometrium of untreated patient is receptive to the fertilized ovum during secretory phase.

Norinyl-1 Patient



Cervical mucus at midcycle is scanty, viscous—with Spinnbarkeit of 1 cm. or less.



Immobile spermatozoa as they appear in cervical mucus taken from patient treated with Norinyl-1.



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Synalar combines the advantage of earlier corticosteroid compounds with unique structural innovations. As a result, preparations of Synalar 0.01% and Synalar 0.025% have been reported to be more potent topically and significantly more effective than hydro-

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The clinical efficacy of Synalar has been extensively documented in the world literature. Commonly encountered diseases such as allergic and contact dermatitis, eczematous and seborrheic dermatitis, and neurodermatitis respond rapidly to Synalar, often

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fluocinolone acetonide





Turn page for contraindications, precautions and side effects.

For everyday topical steroid therapy

Synalar® 0.01%

fluocinolone acetonide

provides economy in two practical dosage forms

For general use, the most economical and widely applicable concentration of Synalar is 0.01% Cream in a water-washable, vanishing cream base. Synalar Solution 0.01% is especially valuable in dermatoses involving moist, intertriginous areas or hairy sites where creams and ointments do not spread or penetrate readily. Synalar Solution is a unique dosage form—clear, nongreasy, cosmetically elegant.

Product Information

Contraindications: Tuberculous, fungal, and most viral lesions of the skin (including herpes simplex, vaccinia, and varicella). Not for ophthalmic use. Contraindicated in individuals with a history of hypersensitivity to any of the components.

Precautions: Synalar preparations are virtually nonsensitizing and nonirritating. However, the solution may produce burning or stinging when applied to denuded or fissured areas. In some patients with dry lesions, the solution may increase dryness, scaling or itching. Where severe local infection or systemic infection exists, the use of systemic antibiotics should be considered, based on susceptibility testing. While topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use on pregnant females has not absolutely been established. Therefore, they should not be used extensively on pregnant patients, in large amounts, or for

prolonged periods of time. **Side Effects:** Side effects are uncommon with topical corticosteroids. As with all drugs, however, a few patients may react unfavorably to Synalar under certain conditions. In such cases the agent should be discontinued and appropriate measures taken.

Availability: Synalar (fluocinolone acetonide) Cream 0.025%—5, 15 and 60 Gm. tubes and 425 Gm. jars. Cream 0.01%—15, 45 and 60 Gm. tubes and 120 Gm. jars. Solution 0.01%—20 and 60 cc. plastic squeeze bottles. Ointment 0.025%—15 and 60 Gm. tubes. Neo-Synalar® (neomycin sulfate 0.5% [0.35% neomycin base], fluocinolone acetonide 0.025%) Cream—5, 15 and 60 Gm. tubes.

fluocinolone acetonide—an original steroid from
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Tumor Conference

Multiple Primary Carcinoma of the Gastrointestinal Tract*

THE SYNCHRONOUS appearance of two primary carcinomas in one patient was first reported in the German literature in 1880 by Czerny¹ and in the English literature in 1888 by Fenger.² Since that time many other reports have appeared in the literature citing cases of multiple primary carcinomas, and several collective series have been reported over the years.^{3,7,8}

From many clinicians and from reading the literature one gains the impression that the incidence of multiple primary carcinomas in a given patient with cancer may be greater than that expected in the general population on the basis of probability alone.

The following case report is presented as an example of a patient who was found to have three simultaneous primary malignant neoplasms of the gastrointestinal tract. The purpose of this case report is to summarize our current thinking on the significance of such a finding.

Case Report

A 64-year-old woman was admitted to the University of Minnesota Hospitals on February 14, 1967, for treatment of a gastric carcinoma. She had been in good health up to the summer of 1966 when she first experienced symptoms consisting primarily of a feeling of abdominal fullness and epigastric pain. She had no history of hematemesis, alteration in bowel habits, melena, or any other symptoms relative to her gastrointestinal tract.

Physical Findings

Physical examination revealed a thin woman who appeared to be in reasonably good general health, and except for a slight elevation of the systolic blood pressure there was no evidence of cardiovascular or respiratory disease. In the abdomen a 4 x 4-cm. ill-defined, firm epigastric mass could be palpated.

Laboratory Studies

Laboratory values revealed an Hgb. of 14.0 Gm., BUN 19 mgm. %, corrected creatinine clearance of 92 L/24 hours, fasting blood sugar of 61 mgm. %, bromsulphthalein of 7% retention at 45 minutes and an alkaline phosphatase of 11 mgm. %. The electrocardiogram was within normal limits.

*Supported by USPHS Grant #CA-08832-01.

Radiological examination of the chest showed no active pulmonary disease. Examination of the upper gastrointestinal tract revealed a gastric lesion extending along the greater and lesser curvature with obvious fixation and rigidity of the gastric wall (Figure 1).



Fig. 1 — Roentgenograph of stomach demonstrating rigidity of wall with lesion involving the body, antrum and pylorus.

Operative Findings

On February 21, 1967, the patient's abdomen was explored through a midline incision. An obvious gastric carcinoma involved the entire stomach except for the distal one inch of antrum and extended almost to the gastroesophageal junction. Along the lesser curvature several nodes appeared to be involved with tumor; however, no spread to the liver or the peritoneal surfaces was observed. The tumor appeared to be amenable to resection for cure.

Prior to resecting the stomach, exploration of the abdomen revealed a napkin-ring type lesion in the ascending colon near the cecum and a second palpable mass circumferentially involving the sigmoid colon. Both of these colonic lesions were felt to be primary carcinomas. No evidence of spread within the pelvis or to local or regional nodes was discovered on careful palpation.

Procedure

A right colectomy with reconstruction of gastrointestinal continuity by an ileotrans-

verse colostomy was done. Similarly, the sigmoid lesion was resected and a descending colostomy performed, using a single layer end-to-end anastomosis.

A total gastrectomy, splenectomy, omentectomy and a nodal dissection were performed, removing the nodes around the hepatic artery, the retropyloric lymph nodes, and the supra-pancreatic lymph nodes, en bloc. The duodenal stump was oversewn. Gastrointestinal continuity was restored by a loop esophagojejunostomy with a distal entero-enterostomy. The abdomen was closed in layers, using wire sutures to approximate the fascia.

The patient tolerated the procedure very well and left the operating room in good condition.

Pathologic Findings

The Ascending Colon Lesion

The ascending colon lesion was a 2½-cm. annular fungating tumor mass located 6 cm. from the ileocecal valve (Figure 2). Histologically it was an adenocarcinoma arising from the surface epithelium and invading deeply into the muscularis externa. Sections of ten small lymph nodes taken from the attached mesentery and connective tissue showed no evidence of tumor.



Fig. 2 — Fungating adenocarcinoma found in the ascending colon, 7 cm. from ileocecal valve.

The Sigmoid Colon Lesion

The resected sigmoid colon contained a 4-cm. annular ulcerated tumor (Figure 3). Three polyps up to 1 cm. in diameter were noted to be in close proximity to the tumor. Sections showed an adenocarcinoma arising from the surface epithelium and extending deeply to the external edge of the muscularis externa. The tumor appeared to be slightly more active and anaplastic than the other colonic lesion. Sections of the polypoid lesions adjacent to the carcinoma revealed adenomatous polyps. There was no evidence of tumor in 19 lymph nodes taken from the mesentery of the resected specimen.



Fig. 3 — Annular carcinoma of the sigmoid colon with three adjacent adenomatous polyps in close proximity.

The Stomach Lesion

The resected stomach measured 27 cm. along the greater curvature and 16 cm. on the lesser, and included 0.5 cm. of duodenum and 1.5 cm. of esophagus (Figure 4). The stomach was thick-walled with a pebbled mucosa, al-

most devoid of mucosal folds. In the anterior wall a shallow 1.5 cm.-ulceration was found in the mucosa. Grossly the tumor seemed to involve almost the entire stomach. It appeared to extend to about 3.5 cm. from the pylorus. Proximally, no gross tumor was seen within 4 cm. of the gastroesophageal junction.



Fig. 4 — Resected stomach with tumor clearly seen on the cut edges with loss of normal rugal pattern.

Histologically the tumor was a diffuse infiltrating adenocarcinoma arising from the surface epithelium and extending all the way through the muscularis externa to the serosal surface. The lines of resection were free of tumor. Sections taken from ten lymph nodes from the gastrohepatic ligament showed five involved with metastatic tumor. The spleen, including six nodes from the splenic pedicle, and the adjacent omentum showed no evidence of tumor.

Postoperative Course

The patient had a benign postoperative course. The wound healed per primum, and she was discharged from the hospital approximately three

weeks after surgery, on March 10, 1967. At the time of her most recent outpatient visit on August 10, 1967, she was found to be essentially asymptomatic, except for a mild diarrhea which is gradually improving. Her appetite is excellent and she is able to maintain her weight, eating four to six meals daily. There is no discomfort after eating and no evidence of bile regurgitation.

Discussion

Since the early reports of multiple primary malignancies, opinions as to the significance of this phenomenon have varied. Basically, three views have been advanced:

Immunity

A prior cancer confers some immunity to subsequent cancer development, and these patients have a lower incidence of new primary carcinomas than the general population.

The theory of active immunization against a malignant tumor was initially proposed by Michaelis in 1907 on the basis of animal experimentation with transplanted tumors.⁴ In 1942 Schmidt reported a series of 3,700 consecutive autopsies with an incidence of multiple primary malignant tumors of only 0.27%.⁵ On the basis of the relative rarity of multiple primary malignant tumors, Schmidt speculated that the possibility of immunity, against the development of a second malignancy in a patient, indeed existed. In another study by Warren and Ehrenreich in 1944, a series of 2,829 autopsies was reported from patients who died from a malignant neoplasm.⁶ They observed an incidence of multiple primary carcinomas of 6.8 per cent and concluded that cases of multiple malignant growths occur more frequently than the expected incidence based on chance alone. They attributed this greater frequency, which they calculated as eleven-fold, to susceptibility or predisposition to cancer in some persons or groups of persons. The major difference in these two reports dealing with large numbers of autopsies naturally resides in the selection of the material under review.

Predisposition

A cancer manifests itself in a group of patients on the basis of some factor or predisposition making them susceptible to the development of cancer, and this group will have a higher than expected incidence of a second or even a third malignancy.

If one is dealing with a group of individuals who are exposed for many years to the influence of carcinogens capable of producing carcinomas in various sites, this particular group undoubtedly will show a higher incidence of those tumors related to the carcinogen. One might expect that if one were to compare the incidence of a second primary cancer in a large group of smokers who have been successfully treated for a carcinoma of the colon, for instance, the chance for subsequent development of a carcinoma of the lung or the oral cavity would be much higher than in a group of non-smokers who had been cured from a similar carcinoma of the colon. A comparable phenomenon of multiple specific histological malignancies is seen in individuals who have been exposed to ionizing radiation. The incidence of carcinoma of the skin and of leukemia is found to be higher in radiologists than in the gen-

eral population of physicians, particularly in the early years before the carcinogenic potential of ionizing radiation was recognized.

Statistical Chance

Multiplicity of primary carcinomas are chance occurrences. Statistical evidence that multiple primary carcinomas are chance occurrences has recently been presented by Spratt and Hoag.⁷ In a group of 4,300 patients seen at the Ellis Fischell State Cancer Hospital from 1940 through 1961 there were 1,130 with colorectal cancer, 710 with carcinoma of the breast, 1,835 with cancer of the cervix, 167 with chronic leukemia and 1,000 without any malignancy at the time of the initial evaluation.

After following these two groups for five years or more, Spratt and Hoag concluded: "The incidence for the development of cancer in the control group and the development of additional cancers after being afflicted with colorectal cancer, mammary cancer, cervical cancer, chronic leukemia, or lymphoma are no greater per man-year of risk. After cervical cancer the number of cancers per man-year of risk and follow-up was significantly less than that in the control group of women of the same median age. Neither the site of a previous cancer nor the absence of a previous cancer influenced site distribution of new cancers." Using data available in the form of life expectancy tables and recognized disease frequency indices, Spratt and Hoag tabulated the probability of a hypothetical population developing carcinomas. Assuming a population of 100,000, all of them living and surviving to age 90, with none succumbing to their first or subsequent cancers, approximately 51% would develop one malignancy, 17% two malignancies, and approximately 6% would have had the time and propensity to develop three malignancies on the basis of probability alone.

Comments

The multiplicity of carcinomas in the colon and rectum has received particular attention in several excellent articles. In 1958 Grinnell reported an incidence of multiple primary carcinoma of the colon and rectum of 5.8% in 1,083 patients seen at the Presbyterian Hospital in New York City between 1916 and 1952.⁸ Diamonte and Bacon have recently reported their experience with synchronous and non-synchronous primary multiple malignancies of the colon and rectum.³ Of 2,508 patients seen with a carcinoma of the colon, 230 patients, or 9.2%, had more than one primary malignancy. One-hundred thirty-four, or 5.2% of the total group of 2,508, had an additional primary carcinoma of the colon. Of these, 80, or 59.1%, were synchronous lesions found at the time of initial evaluation. Of the total group of 230 patients who had multiple primary carcinomas, three had their second primary cancer within the stomach.

The frequency of multiple carcinomas of the colon and rectum is of importance since these tumors are relatively slow-growing lesions and may go undiscovered for long periods of time. Because of the long period of asymptomatic growth, the opportunity to develop a second tumor during this time is greater than in more rapidly growing tumors such as carcinoma of the lung or stomach. This is probably the reason for the higher frequency of multiple synchronous carcinomas in the colon.

In Fenger's initial report in 1888 he described a patient who preoperatively

was diagnosed as having an obstructing carcinoma of the ascending colon.² The patient was operated upon and an ileotransverse colostomy performed. However, the colonic obstruction was unrelenting and the patient died ten days after the surgical procedure. At post-mortem examination he was found to have a second carcinoma completely obstructing the splenic flexure. From this first case recorded in the English literature and from the many cases of multiple carcinomas of the colon and rectum accumulated through the years, it is apparent that three important steps must be taken in treating the patient with a carcinoma. These are:

1. Thorough preoperative evaluation.
2. Thorough intra-operative examination of the areas exposed at the time of surgery.
3. Careful and continuous follow-up, not only to check for any possible recurrence of the initial tumor, but also to reveal the development of additional neoplasms.

Conclusion

From the brief discussion it is evident that our present state of knowledge does not permit us to draw firm conclusions regarding the influence one carcinoma has upon the development of subsequent carcinomas. To a clinician the significance of multiple malignancies is quite clear. The patient with a carcinoma may already have or later develop a second or even a third malignancy.

Peter R. Jochimsen, M.D.*
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*Tumor Clinic, University of Minnesota Medical School, Minneapolis, Minnesota 55455.

References

1. Czerny, V.: Aus der Heidelberger Chirurgischen Klinik. Nachtrag zur Darmresektion. *Klin Wschr* 17:683, 1880.
2. Fenger, C.: Double Carcinoma of the Colon. *JAMA*, 11:606, 1888.
3. Diamonte, M. and Bacon, H.E.: Primary Multiple Malignancy of the Colon and Rectum. *Dis Colon Rectum*, 9:441, 1966.
4. Michaelis, L.: Weitere Experimentelle Untersuchungen uber den Tierkrebs. *Deutsch Med Wschr.* 33:826, 1907.
5. Schmidt, E. A.: Incidence of Multiple Primary Tumors and the Problem of Acquired Cancer Immunity. *Radiology*, 39:208, 1942.
6. Warren, S. and Ehrenreich, T.: Multiple Primary Malignant Tumors and Susceptibility to Cancer. *Cancer Res* 4:554, 1944.
7. Spratt, J. S. and Hoag, M. G.: Incidence of Multiple Primary Cancers per Man Year of Follow-up. *Ann Surg* 164:775, 1966.
8. Grinnell, R. S.: The Rationale of Subtotal and Total Colectomy in the Treatment of Cancer and Multiple Polyps of the Colon. *Surg Gynec Obstet* 106:288, 1958.

On Cosmic Purpose

Is there not something a trifle absurd in the spectacle of human beings holding a mirror before themselves, and thinking what they behold so excellent as to prove that a Cosmic Purpose must have been aiming at it all along? Why, in any case, this glorification of Man? How about lions and tigers? They destroy fewer animal or human lives than we do, and they are much more beautiful than we are. How about ants? They manage the Corporate State much better than any Fascist. Would not a world of nightingales and larks and deer be better than our human world of cruelty and injustice and war? The believers in Cosmic Purpose make much of our supposed intelligence, but their writings make one doubt it. If I were granted omnipotence, and millions of years to experiment in, I should not think Man much to boast of as the final result of all my efforts.*

*Bertrand Russell: Religion and Science.



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**His disturbances at
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Contraindications: Severely depressed or comatose states from any cause, and in association with or following MAO inhibitors; severe hypertensive or hypotensive heart disease.

Precautions: Hypersensitivity reactions (e.g., leukopenia, agranulocytosis) and convulsive seizures are infrequent. Pigmentary retinopathy has been observed where doses in excess of those recommended were used for long periods of time. May potentiate central nervous system depressants, atropine, and phosphorus insecticides. Where complete mental alertness is required, administer the drug cautiously and increase dosage gradually. In addition, orthostatic hypotension (especially in female patients) has been observed. Epinephrine should be avoided in treatment of drug-induced hypotension.

Side Effects: Pseudoparkinsonism and other extrapyramidal disorders are infrequent; drowsiness, especially in high doses early in treatment, may occur; nocturnal confusion, dryness of the mouth, nasal stuffiness, headache, peripheral edema, lactation, galactorrhea, and inhibition of ejaculation are noted on occasion; photosensitivity and other allergic skin reactions may occur but are extremely rare.

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Clinical Path Conference

Valvular Heart Disease and Cardiac Arrhythmia

Dr. Stephen C. Weisberg :*

A sixty-five-year-old male was hospitalized because of an episode of unconsciousness. Three years prior to admission, he had noted syncope. Both episodes occurred after the ingestion of large amounts of beer. Dyspnea after climbing three flights of stairs and an isolated episode of undocumented tachycardia were the only other complaints elicited. Review of systems was non-contributory. A digitalis preparation daily was the only medicine. The blood pressure was 150/100, the pulse 80 and regular. Examination of the head and neck was normal. Wheezes were audible throughout the lung fields. A grade III/VI harsh systolic murmur was audible over the aortic area and radiated into the neck and to the apex. The murmur obscured the heart sounds. No diastolic murmur was heard. The remainder of the examination was normal except for a liver edge palpable 4 cm. below the right costal margin and obesity.

The hemoglobin, wbc. and differential, BUN, urinalysis and serum electrolytes were normal. Cardiac fluoroscopy showed a left ventricular configuration but normal heart size. Calcification in the aortic valve and questionably in the mitral valve was also noted. Electrocardiogram showed a left ventricular strain pattern.

The patient was treated with digitalis and a 1,500 calorie diet, and told to avoid beer.

Fifteen months previously he had been hospitalized for the first time because of exertional and paroxysmal nocturnal dyspnea, two-pillow orthopnea and ankle swelling. These symptoms had been present for one month. The blood pressure was 140/95, the pulse 128 and regular. Examination was normal except for bilateral basilar rales, the previous murmur, 3+ pitting ankle edema, distended neck veins and obesity.

Laboratory evaluation was unchanged. Chest x-ray was compatible with congestive heart failure. Electrocardiogram showed a left ventricular strain pattern.

Bed rest, digitalis and diuretics resulted in a 25-pound loss of weight over seven days, decrease in heart size and symptomatic improvement. These medications were continued on dismissal.

Seven months previously he had been hospitalized because of chest pain. Angina pectoris occurring over a five-year period was described at this time. The substernal chest pain responsible for this hospitalization had lasted 30 minutes. The blood pressure was 110/80, the pulse 140 and regular. Examination showed bilateral basilar rales, the previous murmur, a liver 3 finger-breadths below the costal margin and obesity. Laboratory studies including serial serum glutamic oxaloacetic transaminase were normal. The electrocardiogram was unchanged except for a first-degree heart block and digitalis effect. The patient was dismissed on the fourth hospital day.

The third and final hospitalization was necessitated by an episode of unconsciousness. This episode was preceded by nausea and sweating and was evidently brief. Chest pain was denied. Electrocardiogram on admission showed a supraventricular tachycardia. The blood pressure was 140/80, the pulse 130 and respirations 24. Bilateral basilar rales were again audible. Examination of the heart was unchanged. No edema was noted. The electrocardiogram was reinterpreted as showing a nodal rhythm with atrioventricular dissociation. Chest x-ray was unchanged. Treatment consisted of dilantin 250 mg., seconal 100 mg., Aramine 3 mg. and potassium chloride 40 mEq. in a slow intravenous drip. Two hours later, electrocardiogram showed atrial tachycardia with varying block. Vital signs were stable. Fourteen hours later the patient was found dead.

*Chief Internal Medical Resident, Hennepin County General Hospital.

Dr. Weisberg:

The significant historical features of this patient's illness include: angina pectoris of five years' duration, episodes of syncope, exertional dyspnea and tachycardia. Physical findings include a heart murmur characteristic of aortic stenosis, generalized wheezes and an enlarged liver. Cardiac fluoroscopy and electrocardiography help confirm my clinical impression of aortic valvular disease. The findings on the final hospitalization indicate cardiac failure with associated rhythm disturbances.

Dr. Shih Tsai:*

Review of the films shows concentric hypertrophy of the left ventricle progressing over the period of time the patient was seen to left ventricular enlargement and pulmonary congestion. The aortic valve is calcified. No evidence of post-stenotic dilatation of the aorta is present.

Dr. Weisberg:

I believe the primary disease state to be aortic stenosis. Classification of this valvular disorder is best accomplished by defining the etiology and the location of the stenosis. Etiology may be subdivided into: congenital, bicuspid, senile calcification and rheumatic.

Congenital

The congenital type most often occurs in those patients with a congenital unicuspid valve.

Bicuspid

The bicuspid type may be congenital or acquired. The congenital form will most often lead to calcification of the valve. The acquired form is frequently rheumatic in origin, with fusion of two leaflets, and subsequent calcification. Differentiation of the acquired from the congenital form is often difficult except in rheumatic, when other valves may be involved.

Senile Calcification

The third grouping, that of senile calcification, is often seen. In this form, the base of the valve rather than the edges are calcified, as in rheumatic disease.

Rheumatic

Our fourth type is the rheumatic, where fusion occurs at the edges, without calcification of the valve.

Aortic stenosis in adults is most often calcific and valvular in location. Beyond the age of fifty rheumatic or arteriosclerotic is most common, but congenital bicuspid must also be considered. The calcification in this latter group is usually present by age thirty. Many or most of the patients with calcific aortic stenosis have these changes secondary to wear and tear on the valve, or to an aging or degenerative process. This group will thus have a murmur which will appear after age forty or fifty, as opposed to those with a rheumatic or congenital bicuspid valve in which the murmur will appear at an earlier age. Regardless of the etiology, calcification of the aortic valve occurs with increasing duration of the disease and thus with the age of the patient.

*Chief, Department of Radiology, Hennepin County General Hospital.

History

The history first elicited was that of angina, and we will assume this pain was truly angina and exclude chest pain arising from pulmonary infarction, spontaneous pneumothoraces, pericarditis, dissecting aortic aneurysm or esophageal in origin. These problems would not have appeared over a five-year period or resulted in such a progressive clinical syndrome.

Angina

Angina is a very common symptom and was present five years prior to the patient's demise. Angina is noted in over 20 per cent of patients with aortic stenosis and the incidence increases with age. It is due to functional coronary insufficiency, when the increased demands of the hypertrophic left ventricular myocardium may not be met by the coronary circulation which is perfused at reduced pressure.

Syncope

Syncope is also a common manifestation of aortic stenosis and was noted three years prior to the patient's death. Syncope may be due to a sudden transient cerebral anemia or anoxia caused by an insufficient aortic output. The pathophysiologic disturbance in aortic stenosis is that of left ventricular hypertension not necessarily associated with arterial hypertension, which leads to left ventricular hypertrophy. A tremendously elevated left intraventricular pressure maintains a normal aortic and thus a normal cerebral circulation. However, this exists only with usual restricted activity. A small reserve exists; so with stress the heart cannot compensate for an elevation of pressure and thus a rapid response for increased requirements cannot be met.

Cardiac Asthma

Today, the term "cardiac asthma" is often restricted to those patients, as noted here, in whom wheezes resulting from pulmonary congestion are audible. The combination of an enlarged heart, distended neck veins, hepatic enlargement and peripheral edema indicate right heart failure.

A systolic murmur had always been present in the patient's evaluations and is of extreme importance. Occasionally, a mitral holosystolic murmur due to mitral regurgitation or to ruptured chordae tendinae may radiate to the aortic area and the neck and thus simulate a murmur of aortic stenosis. However, this murmur is holosystolic rather than the diamond-shaped ejection murmur of aortic stenosis. In mitral insufficiency I would expect left atrial dilatation and hypertrophy, which are not apparent in x-rays of this patient, and subsequent left ventricular dilatation and hypertrophy, again not seen. In mitral insufficiency I would expect P wave abnormalities in the electrocardiogram, and this also is not noted in this case.

Aortic Stenosis

The characteristic murmur of aortic stenosis is an ejection-type systolic murmur which is loud, harsh, and of low frequency, with a diamond-shaped crescendo-decrescendo character. It is separated from the first and second heart sounds by a short gap. It is heard at the base and most often will radiate to the neck and apex. Associated findings are a forceful apical impulse,

a systolic thrill at the base, an early systolic ejection click along the left sternal border, an atrial gallop often heard in the apical region, and a slowly rising anacrotic* type of pulse with a narrow pulse pressure.

A diastolic murmur was never noted upon examination. Although this murmur might have been masked, I do not believe it was ever present, for I do not believe aortic insufficiency existed. In aortic insufficiency, left ventricular dilatation always accompanies hypertrophy from the inception; however, in this patient concentric enlargement preceded dilatation.

Sudden death is a common occurrence in patients with aortic stenosis, and most often occurs in those patients in whom syncope and angina have previously occurred. The commonest cause of sudden death is chronic myocardial ischemia with resultant heart failure predisposing to serious arrhythmias. Coronary artery occlusion also occurs in the older age groups. Conduction disturbances are common in patients with aortic stenosis. This may be directly related to extension of calcification from the aortic valve into the region of the node or septum or to progressive cardiac failure.

The electrocardiogram is helpful, but initially may be entirely normal with rapid progression to left axis deviation, left ventricular strain and then hypertrophy.

Radiologic Findings

The radiologic findings in aortic stenosis are often characteristic. In uncomplicated cases in which the heart is well compensated, the overall size of the cardiac silhouette may appear normal when there is concentric hypertrophy, as in this case. The left ventricle does not dilate until late in the course, and then with associated failure. Calcification of the aortic valve is, of course, most essential to the diagnosis. Post-stenotic dilatation, not reported in this case, is found in the proximal portion of the ascending aorta in approximately 50 per cent of cases.

Atrioventricular Dissociation

We are told this patient had a pulse of 130 and an electrocardiogram showing a nodal rhythm with atrioventricular dissociation. If the atrioventricular node activates the ventricles, and the atria are activated by the sino-atrial node, the rhythm is termed atrioventricular dissociation. In this rhythm disturbance the ventricular rate is usually less than 60. Since the pulse was 130, I will assume the rhythm disturbance in the terminal stage was that of interference dissociation. Here the atria and ventricles are controlled by independent pacemakers in the presence of retrograde ventricular-atrial block and intact capacity for adequate antegrade conduction. If the ventricles are regulated by an idioventricular focus, the rate is usually less than 150. Most often this rhythm disturbance is digitalis-induced and is often accompanied by, or precipitated by, an acute myocardial infarction or cerebral vascular accident.

Drug Control of Disease

The treatment consists of removing the causative drug or attempted control of the underlying disease state.

Digitalis

Digitalis, while impairing the conduction of impulses from the atria to

*See Test Your Word Score Page 1823.

the ventricles, partially by vagal stimulation, will most often impair conduction in excess dosage by direct action on the conductive tissues. The treatment for such digitalis-induced and/or similar arrhythmias is not potassium, as was given in this case, because potassium also impairs atrioventricular conduction and will potentiate the degree of block. The irritative effect of digitalis must be considered in a different light from the depressive effect, and the treatment certainly differs.

Aramine

Aramine was also given to the patient and was inappropriate treatment. By raising the blood pressure Aramine stimulates the carotid sinus and aortic receptors with consequent vagal stimulation.

Dilantin

Dilantin was also administered, and this drug, like potassium, may induce further depression and block, and should not have been used. Dilantin may be used to combat the irritative effects of digitalis intoxication. Recent evidence indicates that it may enhance atrioventricular conduction in digitalis-induced atrioventricular block and warrants further study.¹

Treatment

The medical treatment for aortic stenosis is essentially symptomatic. The avoidance of physical activity which surpasses the ability of the patient is indicated. Surgical treatment is indicated for patients with syncope, angina and/or left heart failure and should be that of a prosthetic valve. The surgical mortality today is probably less than 15 per cent. After their first attack patients with progressive cardiac failure have usually less than one year to live without surgery.

Final Diagnosis

I believe the final diagnosis is that of calcific aortic stenosis. I would think we will probably find evidence of a bicuspid valve in this individual. I believe death resulted from progressive cardiac failure and improper treatment of a rhythm disturbance that might have been treated with ethylenediamine-tetraacetic acid. The patient should have been considered for a prosthetic valve after his first hospital admission.

Dr. A. M. Richards:*

I feel it is important in a case of this type to also consider other forms of obstruction such as the subvalvular and supra-ventricular aortic stenoses. I think cardiac catheterization would have been of value in this individual to further define his exact lesion and to rule out the possibility of other existing lesions. However, I do not think that this patient, because of his age, would be a suitable candidate for surgery.

Pathologic Findings

Dr. John T. Crosson:**

At the time of autopsy there was minimal evidence of peripheral edema and no definite cyanosis. On opening the body there was no pleural fluid, and the significant pathology was confined to the heart and lungs.

*Assistant Chief, Internal Medicine, Hennepin County General Hospital.

**Resident in Pathology, Hennepin County General Hospital.

The Heart

The heart was quite enlarged, weighing 700 grams. The left ventricular wall measured 2.5 cm. in width, which is significantly thickened, the normal being about 1.5 cm. The right ventricular wall measured only 0.4 cm., which is within normal limits. The mitral valve, the tricuspid valve, and the pulmonary valves were all normal. The aortic valve was the site of major pathology. It was a bicuspid valve. Both cusps were markedly calcified, the majority of the calcification being at the free edge of the cusp, also extending down along the cusp and even in one place up along the aortic wall as well. However, in this area the calcification did not obstruct the coronary ostia. There was continuity between the right and left cusps, and an abortive raphe, considered to be congenital, was in the mid portion of the right and left cusp where a commissure would have been had this valve developed normally. Figure 1 is a picture of the heart at the time of autopsy, exposing the two aortic cusps and showing the degree of calcification. The coronary ostia appear patent. The left ventricular thickening is also evident. There may be a small jet lesion on the endocardial surface of the left ventricle, suggesting some degree of aortic insufficiency. The coronary arteries were examined and interestingly enough appeared perfectly normal. There were no atherosclerotic changes throughout their distribution, nor was there evidence of any calcific emboli into the coronary arteries.

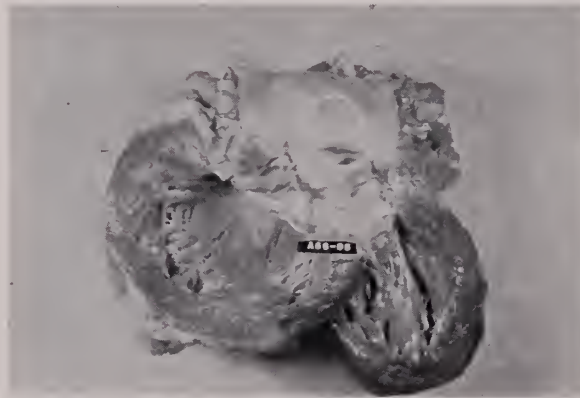


Figure 1



Figure 2

The heart showed evidence both grossly and microscopically of patchy areas of fibrosis but no large unequivocal areas of recent or old infarction. There was evidence of some cardiac muscle hypertrophy on microscopic examination. This heart was also examined by Dr. Edwards who agreed that this probably represented a congenital bicuspid aortic valve which had undergone calcification.

The Lungs

The lungs were markedly congested; the right and left lungs weighed 700 grams and 350 grams respectively. In Figure 2 the severe degree of pulmonary congestion is evident in an external view of the lungs.

The Liver

The liver was slightly enlarged, weighing 2100 grams, but did not show any distinct passive congestion on microscopic examination.

Congenital Bicuspid Valve

Table 1 summarizes some of the factors which would favor the diagnosis of congenital bicuspid valve—some of which apply here and some of which don't. The presence of a congenital raphe, instead of being evidence of previous fusion of two commissures by rheumatic disease, is compatible with a congenital bicuspid valve. The presence of other congenital lesions would support this diagnosis, though no others were detected. The most common anomaly is coarctation of the aorta, but this was clearly absent in this patient. The third factor would be equal cusp sizes. If this was due to rheumatic fusion of the commissures, frequently but not always the cusps would be of unequal size. In this instance, the cusps appear to be relatively equal, suggesting a congenital origin. Finally, the absence of rheumatic disease in the other valves is strongly in support of this being a congenital lesion, although it does not entirely rule out rheumatic involvement.

TABLE I
Factors Favoring Congenital Origin of Bicuspid Valve

A. Congenital Raphe From Valve Leaflet to Aortic Wall
B. Presence of Other Congenital Abnormalities
C. Equal Cusp Sizes
D. Absence of Rheumatic Disease in Other Valves

Rheumatic Valvular Disease

Table 2 summarizes findings that were published by Dr. Paul Dudley White in 1941.² This is a review of some 217 cases of rheumatic valvular disease at the Massachusetts General Hospital and shows the distribution of the valves involved. From his study it is apparent that isolated aortic valve involvement is quite rare. Approximately 70% of patients with rheumatic valvular disease of all sorts will have aortic involvement; however, only 5% of these will have only isolated aortic valve involvement, either aortic stenosis or aortic insufficiency. Dr. Edwards, in theorizing a mechanism for calcification, contrasts the anatomy of the normal tricuspid aortic valve with that of the congenital bicuspid valve. He stresses that in this tricuspid valve the free edges of the aortic valve cusps are longer than the distance between the points of attachment of the cusps on the wall of the aorta. This extra length

to the valve cusp is important in allowing these cusps to open and close without stress. In the congenital bicuspid valve this extra length is not present. The length of the free edge of the cusp in this valve equals the distance between the points of attachment of the cusps on the aortic wall. This allows the aortic valve to open somewhat, but there is some stress and strain put on the valve cusps when opened completely during systole, and the valves then are subject to the trauma of the turbulent blood flow. Sometimes the bicuspid valves will be a little longer than they should be for the distance between the two walls of the aorta. If this is the case, the valves will open normally but not close normally. There will be a prolapse of one or both of the valves with some degree of regurgitation which will then be a source of trauma to the valve. It is Dr. Edward's feeling that this persistent trauma to the collagen bundles in the valve produces a change in the bundles which would be evident if we were fortunate enough to see progressive cases of these diseases. He feels that it is this change which predisposes the valve to the deposition of calcium. He also believes that the same change in the collagen predisposes these valves to the development of subacute endocarditis as well.³

This patient had clinical evidence of myocardial ischemia for some five years prior to his death. However, at the time of autopsy we found no evidence of coronary artery disease. Not infrequently, patients who have aortic stenosis will also have concomitant coronary artery disease which can account for their angina. However, a very significant group of the patients have no coronary disease at all, and this phenomenon of patients with aortic stenosis, angina, and normal coronary arteries has been recognized for quite a few years now. In 1939, Dry and Willius stated that the degree of coronary disease was inversely proportional to the degree of calcific aortic stenosis.⁴ There have been some studies more recently that also support this view. In 1965, Dr. Edwards published a series of cases in which the degree of coronary artery disease for given age groups was compared in patients who had aortic stenosis. From this study he concluded that there was a tendency for lesser degrees of coronary disease to be present in the fifth, sixth and seventh decades in males who have aortic stenosis compared with patients in similar age groups who do not have aortic stenosis.⁵ I think we are seeing an example of this phenomenon in the patient discussed today. Finally, if the coronaries are normal, why do these patients have both clinical and pathological evidence of myocardial ischemia?

TABLE 2
Distribution of Valve Involvement in 217 Cases of
Rheumatic Valve Disease

Mitral Alone	59
Aortic Alone	11
Mitral and Aortic	100
Tricuspid and Mitral	7
Tricuspid, Mitral and Aortic	35
All Four Valves	5

Mechanisms

There has been some discussion by Dr. Weisberg of the mechanisms that might be involved. To me the most reasonable mechanism would relate to the muscular hypertrophy. Because of the marked pressure gradient across the aortic valve, the person who is maintaining a normal pressure in the aorta will have a markedly increased intraventricular pressure, and at the time of

systole, there would be a tremendous increase in pressure on the coronary arteries coursing through the myocardium which would undoubtedly tend to decrease the coronary blood flow. Although this pathogenesis would seem reasonable, a study in *CIRCULATION* in 1965 tended to discount this theory. That study concluded that the coronary blood flow per unit of weight of myocardium in patients with aortic stenosis was the same as in normal patients. In addition, coronary blood flow in these same patients following exercise was found to increase to the same degree as it did in normal patients. These patients with aortic stenosis all had angina, and all manifested clinical evidence of myocardial ischemia.⁶ Therefore, I do not think we yet know the cause of the myocardial ischemia, although we do know that it frequently occurs. We can certainly see pathological evidence of it, and there are many patients cited in the literature who have clinical evidence of ischemia. The presence of syncope, as Dr. Weisberg discussed, is a puzzling matter also but probably not as hard to explain as that of the angina. In 1951, Hammarsten was able to find several cases in the literature in addition to some of his own cases where it was fairly well documented that the syncopal attack suffered by patients with aortic stenosis was associated with decreased cardiac output and normal sinus rhythm or with bradycardia. He found a relationship between angina and syncope in his patients, and he also observed that in some patients the syncopal episode was directly preceded by an attack of angina. He concluded that the syncope was due to decreased cardiac output, and, as Dr. Weisberg indicated, probably due to a sudden episode of myocardial ischemia.⁷ I do not think the mechanism of the sudden myocardial ischemia is understood at all. It seems apparent from the literature, however, that patients with aortic stenosis are prone to develop sudden episodes of myocardial ischemia. If we accept this as being true, I think we can explain the sudden death in many of these patients, because we certainly know that episodes of myocardial ischemia can predispose the myocardium to serious and often fatal arrhythmias.

One final possibility that Dr. Weisberg mentioned that I think worth re-emphasizing is that patients with aortic stenosis do have difficulty with the conduction system. They have varying degrees of heart block which in some cases has been shown to be due to extension of the calcification process directly involving the bundle of His. In this particular case we don't have any studies of the bundle of His, and I don't know whether this man's conduction system was intact or not. However, he did have clinical evidence of condition difficulties which were likely progressive. Failure of the ventricular pacemaker with either asystole or ventricular fibrillation was probably the most likely cause of his demise.

Summary

We have a patient who has a five-year history of episodes of syncope and angina, who has definite clinical evidence of calcific aortic stenosis, who was found at autopsy to have a bicuspid congenital calcific aortic stenosis.

Dr. Fred Shapiro:*

I would appreciate Dr. Weisberg's comment on what drugs might be used in an individual in shock with possible evidence of digitalis intoxication.

*Assistant, Internal Medicine, Hennepin County General Hospital.

Dr. Weisberg:

The patient in this case was not in shock, as the protocol indicated the pressure to have been 140/80. As I indicated before in my discussion, whether the arrhythmia this patient manifested was digitalis-induced or not, ethylenediaminetetraacetic acid may have been indicated, for this drug would not have caused a further depression of the heart's conduction pathways. The drugs employed in this case were of a depressive nature on the conduction system. Dr. Richards, you might wish to comment on what drugs you would recommend for a problem of this type.

Dr. Richards:

We really do not have a good treatment for digitalis intoxication of this sort. I have not been impressed with ethylenediaminetetraacetic acid because of its side effects of nausea and vomiting and have thus tended not to use this agent. I think that today with our present coronary care unit facilities the patient should be monitored and arrhythmias treated as they arise.

Dr. Weisberg:

The problem that arises in this case is the presence of atrioventricular interference association and I feel quite strongly the drugs used were inappropriate and caused further depression on the cardiac conduction system. The only drug that would have been available that would not have caused further depression on the conduction system would have been ethylenediaminetetraacetic acid, and thus I think this drug, if any drug was to be used, might be indicated.

Dr. Shapiro:

I wonder if in this case with such a problem as may have been induced by digitalis, the best treatment would have been no treatment at all.

Dr. Weisberg:

I agree that the most conservative approach would be to withdraw the drug which might be precipitating such an arrhythmia. In this case, we of course realize the underlying organic heart disease may have been the major factor in contributing to the arrhythmia, and digitalis may or may not have been an important precipitating effect.

Dr. Thomas Stillman:

I agree with Dr. Weisberg that the irritative and depressive effects of digitalis must be separated and recognized and that their treatment does differ, as he has indicated.

Stephen C. Weisberg, M.D.
John T. Crosson, M.D.
Hennepin County General Hospital

References

1. Helfant, R. H., et al.: *Circulation* 36:108, 1967.
2. Cooke, W. T. and White, P. D.: *Brit Heart J* 3:147, 1941.
3. Edwards, J.: *Circulation* 26:817, 1962.
4. Dry, T. J. and Willius, F. A.: *Amer Heart J* 17:138, 1939.
5. Edwards, J., et al.: *Arch Path* 80:517, 1965.
6. Row, G. G., et al.: *Circulation* 32:251, 1965.
7. Hammarsten, J. F.: *Arch Intern Med* 87:274, 1951.

Functions

In illness the physician is a father; in convalescence, a friend; when health is restored, he is a guardian.—Brahmanic saying

Nail Dystrophies

A 25-YEAR-OLD woman sought help for a nail abnormality of five years' duration. Without illness or other apparent cause a groove developed in her thumb nail, extending from the lunula to the free edge. The condition lasted approximately six to 12 months; then the nail would resume a normal pattern of growth. The condition recurred; first one thumb nail then the other would become involved. She was in good health with a past medical history which was noncontributory and there were no occupational or other forms of trauma to account for these changes. A diagnosis of *dystrophia mediana canaliformis* was made (see Figure).

When abnormal and deformed in any way, the nails may be a source of considerable concern to a patient and a cause for frustration on the part of the physician to whom the problem is presented. Nail dystrophies (onycho-dystrophies) are diverse affections which may be secondary to various pathologic states or of unknown cause. The present case illustrates one of the rare dystrophies which apparently have no definite local or systemic cause. Trauma as well as a nervous origin have been implicated. However, the condition is benign and any treatment should be conservative.

Another benign and very common dystrophy is *leukonychia*.* In this affection one or more white puncta or striae occur transverse to the axis of the

*See Test Your Word Score Page 1823.



Figure

nail plate. Rarely is the nail totally involved (leukonychia totalis). The fingernails are most commonly affected. This condition is not symptomatic of systemic disease. Trauma as well as imperfect or faulty cornification have been considered possible causes.

Hypertrophy of the nail is called *onychauxis*, the toe nails being more commonly involved. If the nail becomes claw-like the term *onychogryphosis* is used. These abnormalities occur in aged ill-kept individuals and at times in association with peripheral neuritis, stasic changes, hemiplegia, ichthyosis, tabes, or leprosy. Subungual hyperkeratosis may occur with these dystrophies, as well as with psoriasis, eczema and fungal disease. This latter point is well to keep in mind, for not all thickened nails are due to a mycotic infection.

Separation of the nail from its bed or matrix is another common dystrophy. When the nail separates distally it is termed *onycholysis*, while if the separation occurs proximally the term *onychomadesis* is applied. *Onycholysis* has been attributed to eczema, psoriasis, syphilis, trauma (both mechanical and chemical). *Onychomadesis* has been associated with scarlet fever, alopecia areata, exfoliative dermatitis, trauma and infections around the nail bed. Also hereditary examples of these dystrophies occur.

Of those dystrophies associated with systemic disease, *koilonychia* or "spoon nail" is a good example. This condition has been reported with various anemias, including Plummer-Vinson syndrome, and with thyrotoxicosis, polycythemia vera and trauma. Another example is Beau's lines, which are transverse sulci appearing at the lunula and progressing to the free edge. These were first described by Beau in 1846 as an indication of previous disease or trauma.

This discussion by no means exhausts all the various nail dystrophies but does point out the diverse way this epithelial appendage can respond to known and unknown factors. Treatment is directed toward the underlying disease, if it can be determined; otherwise treatment should be conservative.

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Minneapolis, Minnesota

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Minnesota Medicine Cover Photographs

In order to encourage more physicians to submit color slides for use on the cover of MINNESOTA MEDICINE the competition is being discontinued. The picture editor now invites all physician-photographers to send 35 mm. color slides of suitable subjects for consideration as cover pictures. The format must be horizontal because of printing limitations. Pictures high-lighting Minnesota seasons, places, and activities will have an automatic advantage. No limit as to the number of slides sent will be set, but all slides should be individually identified. All slides will be returned. Physicians whose pictures are used as covers will be recognized in MINNESOTA MEDICINE. We can use many more pictures than we have received in the past.

I can reason down or deny everything, except this perpetual Belly: feed he must and will, and I cannot make him respectable.—Emerson

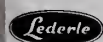
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Precautions—Overgrowth of nonsusceptible organisms may occur. Constant observation is essential. If new infections appear, appropriate measures should be taken. In infants, increased intracranial pressure with bulging fontanels has been observed. All signs and symptoms have disappeared rapidly upon cessation of treatment.

Side Effects—Gastrointestinal system—anorexia, nausea, vomiting, diarrhea, stomatitis, glossitis, enterocolitis, pruritus ani. Skin—maculopapular and erythematous rashes. A rare case of exfoliative dermatitis has been reported. Photosensitivity; onycholysis and discoloration of the nails (rare). Kidney—rise in BUN, apparently dose related. Transient increase in urinary output, sometimes accompanied by thirst (rare). Hypersensitivity reactions—urticaria, angioneurotic edema, anaphylaxis. Teeth—dental staining (yellow-brown) in children of mothers given this drug during the latter half of pregnancy, and in children given the drug during the neonatal period, infancy and early childhood. Enamel hypoplasia has been seen in a few children. If adverse reaction or idiosyncrasy occurs discontinue medication and institute appropriate therapy.

Average Adult Daily Dosage: 150 mg q.i.d. or 300 mg b.i.d. Should be given 1 hour before or 2 hours after meals, since absorption is impaired by the concomitant administration of high calcium content drugs, foods and some dairy products. Treatment of streptococcal infections should continue for 10 days, even though symptoms have subsided.

In the treatment of syphilis a dosage schedule of a total of 12 to 18 Gm. given in equally divided doses over a period of 10 to 15 days should be followed. Close follow-up observation of the patient is recommended, including appropriate laboratory tests, since demethylchlortetracycline has not had adequate evaluation in all stages of syphilis. Spinal fluid examination should be included as part of this follow-up.

Acute gonococcal anterior urethritis in males has been treated effectively with a single dose of 600-900 mg. of DECLOMYCIN Demethylchlortetracycline. Individuals unable to tolerate large single doses due to gastrointestinal side effects may be treated with 150 mg. every 6 hours for a minimum of 4 doses or 300 mg. every 12 hours for a minimum of 2 doses. Females should be treated with a dosage of 150 mg. every 6 hours or 300 mg. every 12 hours until a cure is affected. Primary Atypical Pneumonia (Eaton Agent): The average adult daily dosage is 900 mg. in 3 divided doses for six days.

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Grand Rounds

Polycythemia Vera*

OLE JERDE, M.D.
Medical Resident

Etiology

POLYCYTHEMIA VERA is a disease of unknown etiology which is characterized by a pancytosis** of the bone marrow. Various theories including hypoxia of the bone marrow and possible hormonal cause have been postulated; however, it is now considered to be a neoplastic disease.¹ Dameshek² feels that polycythemia vera is one of the myeloproliferative diseases which include chronic granulocytic leukemia, agnogenic** myeloid metaplasia of the spleen, megakaryocytic leukemia, and erythroleukemia. He states that 10 to 20% of patients with polycythemia vera, unless dying early in their disease, will develop anemia with a "leuko-erythroblastic" blood picture and will have myeloid metaplasia of the spleen in addition to myelofibrosis. The myeloid metaplasia with splenomegaly may begin before there is fibrosis in the bone marrow, indicating that this is not a purely compensatory extramedullary hematopoiesis. While these diseases may be independent entities, there are numerous case reports in the literature of transition from one to the other. Wasserman¹ studied 61 cases of myelofibrosis with myeloid metaplasia and found that 58% of these patients had a history suggestive of polycythemia vera. In chronic granulocytic leukemia, especially early in the course of the disease, erythrocytosis and thrombocytosis are commonly present. There are three case reports in the literature in which erythroleukemia followed polycythemia vera.³ These authors speculate that P_{32} therapy may have been a factor. Erythropoietin, a humoral substance produced in the kidneys and possibly other tissues, is important in the genesis of polycythemia secondary

*Presented as a Medical Grand Rounds at Hennepin County General Hospital, Minneapolis, April 18, 1967.

**See Test Your Word Score Page 1823.

to other diseases; however, it does not appear to play a role in polycythemia vera.⁴

Clinical Features and Differential Diagnosis

The onset of polycythemia vera is gradual and the complaints and symptoms may be varied. Patients often complain of headaches, aches and pains throughout the body, visual disturbances, loss of memory, fatigability, and dyspnea on exertion.⁵ Dizziness is quite common and has been reported in over 10% of patients.⁶ In a third of a series of 250 patients the first signs and symptoms were related to hemorrhage or thrombosis, illustrating one of the complications of this disease (Table 1).⁶ Other manifestations include itching, gait disturbances, paresthesias, and gastrointestinal complaints. In Lawrence's series⁵ 19% of the patients had peptic ulcer disease. While the incidence in other series is less than this, ulcer disease is common in polycythemia vera.⁷ The plethoric, ruddy face is quite characteristic of this disease. Hepatomegaly is present in 25⁵ to 50%⁹ and splenomegaly in 75%⁹ of the cases.

TABLE 1*
First Symptom or Sign—250 Patients

	No. of Patients
Dizziness	28
Headache	5
Itching	7
Dysbasia	6
Paresthesias	1
Dyspepsia	24
Angina pectoris	8
Polycythemic coloring	35
Splenomegaly—splenic pain	17
Gout	10
Thrombophlebitis of the extremities	19
Cerebral thrombosis	28
Coronary thrombosis	7
Epistaxis or gingival bleeding	11
Hematuria	1
Hemoptysis	2
Suggillations	2
Hematemesis-melena	13
Accidental findings	26

*Chievitz, E., and Thiede, T.: *Acta Med Scand* 172:513, 1962.

The differential diagnosis of polycythemia vera includes the following disorders:⁹

Secondary polycythemia
 "Stress" polycythemia
 Erythropoietin polycythemias
 Polycythemia with tumors
 Primary erythrocytosis (See Tables 2 and 3)

"Stress" polycythemia, pseudopolycythemia,¹⁰ or Gaisbock's disease¹¹ can be easily confused with polycythemia vera. The patients have ruddy faces and complaints suggestive of polycythemia vera. They are of stocky build, slightly obese, often hypertensive and frequently rather nervous and anxious-appearing. The venous hematocrit and hemoglobin are elevated; however, the platelet and leukocyte counts are normal. Isotope studies reveal a normal red-cell mass with a decreased plasma volume which accounts for the

elevated hematocrit reading. This is a chronic problem and patients have been followed for ten years with no change in the blood-volume studies, clinical picture, or blood morphology.¹¹ It is important to distinguish this disease from polycythemia vera since phlebotomies are of questionable value and therapy with P₃₂ is contraindicated.^{11,12} The etiology of "stress" polycythemia is unknown.

Secondary polycythemia is due to a low arterial blood oxygen saturation. This occurs in patients with congenital heart disease, severe pulmonary disease, and in people living at high altitudes. It also occurs in the Pickwickian syndrome and in diseases with impaired oxygen transport.⁹ Clinically there should be little difficulty in distinguishing this group from polycythemia vera (Tables 3, 4 and 5).

TABLE 2*

Polycythemia vera
Secondary polycythemia—including Pickwickian syndrome
"Stress" polycythemia
Erythropoietin polycythemias (with normal blood O ₂ saturation):
cerebellar hemangioblastoma
renal cancer
renal adenoma
hydronephrosis
renal cysts
Polycythemia with tumors (erythropoietin not demonstrated):
adrenocortical carcinoma or hyperplasia
ovarian carcinoma
hepatoma
pheochromocytoma
Primary erythrocytosis (of childhood)—benign familial polycythemia

*Berlin: Seminars in Hematology, p. 209, July 1966.

TABLE 3*
Differential Diagnosis of Polycythemia Vera: History and Examination

Polycythemia Vera	Stress Erythrocytosis	Anoxemic Erythrocytosis	Tumor Erythrocytosis
History			
Multiplicity of symptoms	Symptoms of nervous tension	High altitude	History may be lacking or related to tumor
Peptic ulcer (20%)	Peptic ulcer, common	Chronic lung disease Congenital heart disease	
Gout occasionally	Gout occasionally	Extreme obesity (Pickwickian syndrome)	
Severe itching skin after bathing (50% of cases)	No itching of skin after bathing	No itching of skin after bathing	No itching of skin after bathing
Physical Examination			
Plethora of skin and mucous membranes	± Plethora of skin; mucous membranes normal	Cyanosis	No cyanosis, clubbing, heart or lung disease
Distention of retinal veins	Retinal veins normal	Clubbing of fingers ±	Occasional mass in left upper quadrant or in pelvis
Hepatomegaly (50%)	Occ. hepatomegaly Acrocyanosis common		
Splenomegaly (75%)	No splenomegaly	No splenomegaly	No splenomegaly

*Dameshek, W.: Seminars in Hematology, 3:214, 1966.

Another group of patients may present with polycythemia and with study will be found to have benign and malignant conditions accounting for it. Cerebellar hemangioblastomas are a common cause in this group. In a review of the literature Waldmann et al.¹³ found that a polycythemic syndrome was present in 9 to 20% of these tumors. Bone-marrow biopsies, when performed, generally showed erythroid hyperplasia, and red-cell volumes were usually increased. Arterial oxygen studies were generally normal. Fluid removed from the cyst was injected into rats and gave rise to an increase in erythropoiesis as determined by radioactive iron studies. When the tumor is resected, the patient's hemoglobin quickly returns to normal, but rises again with recurrence of the tumor. It would appear that these tumors secrete a substance that gives rise to erythropoiesis.

Various kidney lesions can also produce a polycythemic picture. These include hypernephromas, hydronephrosis, benign adenomas, and renal cysts.^{8,9,14,15} Erythropoietin has been found in most of these lesions with clinical remission of the syndrome postoperatively.

TABLE 4*
Differential Diagnosis of Polycythemia Vera: Blood and Bone Marrow

Polycythemia Vera	Stress Erythrocytosis	Anoxemic Erythrocytosis	Tumor Erythrocytosis
Blood:			
Hgb. ++ (to 20 Gm)	+ (to 17 Gm)	+ to +++	+
RBC +++ (7-12 M)	+ (to 6.5 M)	+ to +++	+
Hct. 60-80%	50-55%	50-80%	50-60%
Retics. + (12-6%)	Normal	Normal or slight +	Normal or slight +
Wbc. + (12-20 ³)	Normal	Normal	Normal or slight +
Platelets ++ (2-10 ⁶)	Normal	Normal	Normal
Polys +	Normal	Normal	Normal or slight +
Bands +	Normal	Normal	Normal or slight +
Occ. myelocyte	No myelocytes		
Occ. nucleated RBC.	No nucleated RBC.		
Bone Marrow:			
Wbc. ++	Erythrocytosis- no pancytosis	Erythrocytosis- no pancytosis	Erythrocytosis- no pancytosis
Wbc. ++	Normal	Normal	Normal
Megas +++			
Sed Rate: 0-1	Normal (10-20)	Normal or low	

*Dameshek, W.: *Seminars in Hematology*, 3:214, 1966.

TABLE 5*
Differential Diagnosis of Polycythemia Vera: Special Tests

Polycythemia Vera	Stress Erythrocytosis	Anoxemic Erythrocytosis	Tumor Erythrocytosis
Leukocyte Alkaline Phosphatase			
+++ (almost invariably)	Normal	Normal	Normal
Blood Volume			
Red cell mass ++	Normal	+ to ++	+ to ++
Plasma Volume			
Normal or slightly +	Reduced	Normal	Normal
Arterial O₂ Saturation			
Normal	Normal	Reduced	Normal
IV Pyelogram			
Normal	Normal	Normal	May show renal tumor

*Dameshek, W.: *Seminars in Hematology*, p. 214, July 1966.

Hepatomas of the liver,¹⁶ as well as one case of a hamartoma of the liver,¹⁷ have been reported to cause polycythemia. Many of these patients had underlying cirrhosis of the liver. Following removal of the hamartoma the patient's hemoglobin returned to normal and remained there during a one-year follow-up. An erythropoietic-stimulating substance was not demonstrated but was presumed to be present. Berlin⁹ notes other tumors that have also caused polycythemia.

In general, the exact diagnosis of most polycythemic conditions can be made on the basis of history, physical examination, peripheral blood studies and bone marrow examination. Other laboratory procedures to be done include the sedimentation rate, which tends to be very low in polycythemia vera but may also be low in anoxemic conditions, and oxygen saturation studies to delineate the anoxemic group. The red-cell mass study will be normal in "stress" erythrocytosis but is elevated in the other types.⁸ Radioactive iron studies will be normal in "stress" erythrocytosis but is elevated in all conditions in which there is erythroid hyperplasia.¹⁸ The leukocyte alkaline phosphatase is generally markedly elevated in polycythemia vera and appears to be a reliable test for separating polycythemia vera from the other three groups. This substance, however, may be elevated in other blood dyscrasias also.¹⁹

Course and Complications

The natural course of polycythemia vera is not well known since therapy is usually instituted as soon as the diagnosis is made. Most investigators agree with Wasserman and Gilbert²⁰ that the "erythrocytic phase" occurs first and is characterized by proliferation of the erythroid cells as well as other cell lines. Assuming the patient survives this phase of the disease, he may enter the "spent phase," which again may last for years and is characterized by decreased erythroid activity and anemia. Myelofibrosis and myeloid metaplasia may occur in this "spent phase".²⁰

Chievitz and Thiede⁶ reviewed the case records of 250 deaths in patients who had polycythemia vera, one hundred eleven of whom were untreated or treated with venesection alone. Of those untreated approximately 50% died within 18 months. Of those treated by venesection alone, 50% died in about 3½ years. However, of these 111 cases, 36 were alive at the five-year

TABLE 6*
Causes of Death

	No. of Patients
Thrombosis or emboli	100
Hemorrhage	15
Leukemia-myelofibrosis-anemia	25
Cirrhosis of the liver	3
Urinary tract diseases (incl. cancer in 3)	20
Heart diseases (excl. coronary thrombosis)	21
Cancer (excl. cancer of the urinary tract)	9
Bronchopneumonia	14
Cerebral hemorrhage	8
Senility-debility	6
Accidents, suicide	7
Postoperative	5
Miscellaneous	7
Uncertain or unknown cause	10
Total	250

*Chievitz and Thiede: Acta Med Scand 172: c. 5: 514, 1962

follow-up and 15 at 10 years. In Videbaek's series⁷ of 125 patients who were treated by various means other than P_{32} the average duration of the disease was six years in male patients and nine in female.

Hemorrhage and thrombosis in the untreated patient is the most common cause of death and accounted for 123 deaths in Chievitz and Thiede's series⁶ (Table 6). Sixty-three per cent of the deaths in untreated patients were due to thrombosis, while 52% of those treated by venesection alone died of thrombosis.

Polycythemia vera is unusual in that both hemorrhage and thrombosis are very common. The fibrin network appears to be more friable than usual with "fallout" of red cells, even though the platelet counts are normal or elevated.²¹ These authors also noted a qualitative defect in platelets. Sheehy et al.²² postulated that a triad consisting of (1) excess abnormal platelets, (2) increased red cell mass, and (3) fibrinogenopenia probably accounted for hemorrhage. Wasserman and Gilbert²³ found a defect in the platelet fibrin network. Further studies revealed a defect in 5-hydroxytryptamine in 50% of the patients they studied.

As mentioned previously, peptic ulcer is quite common and occurs in up to 20% of polycythemia vera patients.⁸ This, plus the bleeding problem already present, makes gastrointestinal bleeding a common and serious problem.

Hyperuricemia has been noted in up to 80% of patients with either untreated or "spent" polycythemia vera and myeloid metaplasia.²³ Gout is much less common but occurs in 6²⁴ to 13%.⁶ Other complications include, pathological fractures, pancytopenia, nephrolithiasis, splenic infarcts, and hemolysis.²⁰

Treatment of Polycythemia Vera

Patients may present with erythrocytosis and may be relatively asymptomatic. Gardner²⁵ recommends repeated phlebotomies to reduce the hematocrit to 42%. If the hematocrit can be maintained in this range by no more than six phlebotomies per year, he would not use other therapy. This produces a mild iron deficiency which retards erythropoiesis. Platelet counts should be followed closely, since repeated phlebotomies may stimulate the bone marrow, producing a thrombocytosis.²⁰ Most patients, however, will need myelosuppressive therapy, using either P_{32} or various drugs.

Radioactive phosphorus was first used in the treatment of this disease by Lawrence²⁶ in 1940 and has been widely used since. P_{32} will give good results in most patients. Lawrence⁵ reported a 90% incidence of remissions. Ledlie²⁷ reported satisfactory results with clinical remissions lasting up to 22 months. Szur and Lewis²⁸ reported good to partial responses in 96% of the patients in their series of 169 cases. In 90% or more of patients, P_{32} will produce a clinical remission, with improvement in the patient's symptomatology in addition to improvement in the blood picture. Lawrence⁵ recommended using small doses of P_{32} and reported no serious bone-marrow depression. He preferred using 3 millicuries intravenously, followed by phlebotomies, if necessary, to reduce the red-cell mass with re-evaluation and a similar dose of P_{32} , if necessary, in three months. It occasionally took one to two years to induce a remission; however, the disease was usually under control during this period of time. Generally 3 to 6 millicuries of P_{32} are given initially, the dose tending to be proportional to the severity of the disease. Platelet and white cell counts tend to be easily controlled with this drug; however, phlebotomies may be needed to help control the red cell count. Another

favorable factor with P_{32} is the convenience for the patients. After a remission they need less frequent clinic visits and blood studies compared with patients taking drugs.²⁵ P_{32} effectively controls the disease for many years. Several authors^{5,29,30,31,32} report a median survival of 13 years after therapy.

The main complication of P_{32} centers around the relationship of polycythemia vera and acute leukemia. There are numerous case reports describing the transition of polycythemia vera to acute leukemia. Schwartz and Ehrlich³³ in 1950 reviewed the literature concerning these two diseases and rejected all but 30 case reports. Most of these patients had been treated by X-ray therapy, P_{32} , or both. The authors concluded that when acute leukemia occurred in polycythemia vera patients it was due to irradiation. Halnon and Russell²⁹ in a large series all treated with X-ray therapy or P_{32} found no cases of acute leukemia. Ledlie's series²⁷ in which all were treated with P_{32} reported five of 21 deaths to be due to acute myeloid leukemia. One of his patients had immature white blood cells in the peripheral blood and all had had white blood counts greater than 10,000 before therapy. These patients all developed their leukemia within four years of therapy. Masouredis and Lawrence³² noted that the patients who developed acute leukemia had had higher white blood counts, higher platelet levels and more immature cells in the peripheral smear before treatment. They postulated that the leukemia potential was present before therapy and that P_{32} served to trigger it. In Osgood's series³⁰ the patients treated with P_{32} survived longer than those under other methods of therapy, and he theorized that leukemia might be a natural complication in those patients who survived long enough to get the disease. Modan and Lilienfeld³¹ found an incidence of 11% acute myeloid leukemia in patients treated with P_{32} and less than 1% in the non-irradiated group. Prolonged survival did not seem to be the answer since there was little difference between the irradiated and the non-irradiated group. The onset of leukemia was not related to time but was related to the total dose given. Fifty per cent of patients had the onset of acute leukemia within the first eight to nine years after therapy.

Busulfan, an alkylating agent, is one of the commonly used drugs giving good results. Wald et al.³⁴ reported five patients treated with Busulfan with good clinical results in all. He noted a significant reduction in white blood cell, red blood cell and platelet counts with remissions lasting three to 20 months. Killman and Cronkite³⁵ used Busulfan on 12 patients with good response in all. Platelet and white cell counts were significantly reduced with less reduction in the red-cell mass which could be controlled by an occasional phlebotomy. Louis³⁶ reported 18 patients treated with Busulfan with complete remission in 11 patients and incomplete remission in six others. Patients required close observation since there was a marked variation in the individual dosage.

Pyremethamine, a folic-acid antagonist, has been used in England with good clinical results. Megloblastic anemia was a common side effect but was easily corrected by decreasing the dose or adding folic acid.

Cyclophosphonide and chlorambucil have been used with good clinical responses.²⁰

Perkins et al.³⁷ report a series of 127 patients treated with a variety of drugs and/or venesection with a median survival of 13.6 years. They have not observed any cases of acute leukemia.

Vercyte is a very effective drug in the treatment of polycythemia vera.^{38,39} Red-cell mass, white blood cell and platelet counts are effectively controlled

on low doses. While there may be some cases of bone-marrow depression, these have all been reversible. No cases of leukemia have been reported. Diarrhea may be a problem and one patient was unable to tolerate the drug because of this.³⁹

Case Report

A 74-year-old white male was admitted to Hennepin County General Hospital on December 9, 1966, because of weakness and difficulty in walking for about six weeks. His knees would "buckle" and he would fall. He had been getting worse, and on the day of admission he had fallen and been unable to get up.

The patient had been hospitalized here in April, 1965, following a syncopal attack. Hgb. 21.5 and 23, HCT. 66, wbc. 13,900, platelet count 330,000. He had signed out, however, against medical advice before studies could be completed.

The patient was a well-developed, slightly lethargic, ruddy-faced white male. B.P. 130/70, P. 96, R. 26. EENT-Fundi showed some ruddiness with mild venous congestion but no pulp edema. Heart normal. Lungs normal. Abdomen-liver edge two finger-breadths below right costal margin. Spleen not palpable. Extremities-moderate cyanosis of toes and fingers. Neurological-trunkal ataxia with dysnergia and dysmetria of lower extremities.

Hgb. 24.4 gm.%, HCT. 71.5%, wbc. 13,500/mm³, 90% neut., 6% lymph., 1% mono., 3% eos., RBC 7.07 million/mm³, platelet estimate 258,000/mm³, reticulocyte count 0.9%, E.S.K. 0 mm/hr. uric acid 9.0 mg.%, chest X-ray normal, electrocardiogram left axis deviation.

A neurological consultation was obtained and the impression was that the neurological picture was due to ischemia of the brain stem. The patient was treated with phlebotomies at about 400 cc. daily. On December 14, 1966: Hgb. 23.4, HCT. 68, wbc. 14,000, platelet count 318,000, blood vol. 7,100 cc., pH. 7.50, PO₂ 72 mm. Hg.-95.9% saturation, PCO₂-29.

The patient gradually became more lethargic and somnolent and developed paresis of the left upper arm and both lower legs. IVP showed some fibrolipomatosis but was otherwise normal. Brain scan was non-diagnostic. Electrocardiogram was interpreted as mildly abnormal with paralysis of left arm and extreme paresis of both lower legs. He then developed thrombophlebitis of the right lower leg extending to the groin and was started on heparin. On January 3, 1967: Hgb. 16.9, platelet count 466,000. Shortly after starting heparin the patient's thrombophlebitis improved along with slow but steady improvement in his neurological picture. A bone marrow, done on January 29, 1967, showed hypercellularity and a slight decrease in iron stones and was compatible with polycythemia vera. The patient was given 5 millicuries of P₃₂ IV and discharged on dicumarol to the care of his private physician.

References

1. Wasserman, L.: Bull NY Acad Med 30:343, 1954.
2. Dameshek, W.: Blood, 6:372, 1951.
3. Bank, A., Larson, P., and Anderson, H.: New Engl J Med 275:489, 1966.
4. Stohlman, F.: Seminars in Hematology, 3:181, 1966.
5. Lawrence, J., Berlin, N., and Huff, R.: Medicine, 32:323, 1953.
6. Chievitz, E., and Thiede, T.: Acta Med Scand 172: 513, 1962.
7. Videbaek, A.: Acta Med Scand 138:179, 1950.
8. Dameshek, W.: Seminars in Hematology 3:214, 1966.
9. Berlin, N.: Seminars in Hematology 3:209, 1966.
10. Kaung, D., and Peterson, R.: Arch Intern Med 110:456, 1962.
11. Russell, R., and Conley, C.: Arch Intern Med 114: 734, 1964.
12. Halls, C.: Arch Intern Med 116:4, 1965.
13. Waldman, T., Levin, E., and Baldwin, M.: Amer J Med 31:318, 1961.
14. Lawrence, J., and Donald, W.: Ann Intern Med 50: 959, 1959.
15. Rosse, W., Waldmann, T., and Cohen, P.: Amer J Med 34:76, 1963.
16. Brownstein, M. and Ballard, H.: Amer J Med 40: 204, 1966.
17. Josephs, B., Robbins, E., and Levine, A.: JAMA 179:867, 1962.
18. Bothwell, T., Callender, S., Mallett, B., and Witts, L.: Brit J Haemat 2:1, 1956.
19. Mitus, W., Mednicoff, I., and Dameshek, W.: New Engl J Med 260:1131, 1959.
20. Wasserman, L., and Gilbert, H.: Med Clin N Amer 50:1501, 1966.
21. Abraham, J., Ulutin, O., Johnson, S., and Caldwell, M.: Amer J Clin Path 36:7, 1961.
22. Sheehy, T., and Montalvo, G.: Amer J Med Sci 243:183, 1962.
- 23-39. May be secured from the author or the reprints.

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* * * *

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* * * *

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* * * *

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* * * *

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Utopia?

Oscar Wilde once said: "A map of the world on which the country of Utopia is not marked deserves no glance, for it leaves out the shores on which mankind will eternally land. And when mankind arrives there, it looks around for a better land and sets sail for it."

The Semisynthetic Penicillins

THE SUBJECT of the semisynthetic penicillins has been reviewed previously.¹⁻⁴ The present report represents an effort to bring this subject up to date. The sharing of 6-amino-penicillanic acid (6-APA) as a nucleus, cross-allergenicity, and a bactericidal effect on susceptible microorganisms characterize the group of antibiotics known as the penicillins. The penicillins appear to act by interfering with the transfer of muramic acid and the subsequent synthesis of mucopeptides that are essential for the formation and integrity of the cell walls of susceptible microorganisms. These drugs apparently act only on growing cells and appear to be inactive against resting microorganisms.⁵

The naturally occurring penicillins are produced by fermentation of several species of molds, including *Penicillium notatum* and notably a strain of *Penicillium chrysogenum*. On identification of the penicillin nucleus, the semisynthesis of the penicillins became possible, and the clinical characteristics of these drugs reflect the chemical addition of various side chains to the 6-APA nucleus.

Of the naturally occurring drugs, penicillin G generally is preferred to penicillin V in more serious infections. With the recognition of cross-allergenicity, penicillin O is no longer commonly used. There are other natural penicillins such as F, K, N, and X, which have no current clinical application. In general, infections previously responding to penicillins G and V continue to respond, except those due to certain staphylococci.^{6,7}

The natural penicillins eluded chemical identification until 1958, when Seehan constructed the penicillin nucleus, 6-APA, a fused beta-lactamthiazolidine ring system that has a carboxyl group at carbon 3 and an amino group at carbon 6. The molds, which produce the natural penicillins, produce the nucleus before attachment of the side chains. Procedures were

developed that inhibited attachment of the side chains, thus stopping production of the molds just after the unattached nucleus had been produced. The fermentation process was scaled up in order to produce 6-APA in large quantities, and organic chemists began adding various side chains. An alternative method for producing 6-APA is employment of amidase (acylase) enzymes to remove the side chain from readily obtainable penicillins. These penicillinamidases or penicillinacylases are of fungal and bacterial origin.⁸

The first commercial example of the semisynthesis of penicillins was phenethicillin, but a more monumental accomplishment was the semisynthesis of the penicillinase-resistant methicillin in 1960 by Doyle. Further search has led to other semisynthetic penicillins, but these drugs appear to be only bellwethers of even newer derivatives that have possible clinical application.

The preparations of the penicillins are available for oral and parenteral administration, but their topical application should be avoided. This is so because indications for their topical use are virtually nonexistent, and consequent hypersensitization to the penicillins, when used in this fashion, is not infrequent. Also, despite considerable speculation, it is not known whether a constant level of these drugs in serum is more or less effective than a varying concentration. As a generalization, the penicillins enter ascitic fluid and cross the placental barrier, but their diffusion into body cavities and fluids is poor unless they are given in large doses or inflammation is present. Compared to methicillin, oxacillin may be characterized by its relative inability to diffuse into some body cavities and fluids.

Phenethicillin (Phenoxyethyl Penicillin)

Phenethicillin (Syncillin, Darcil, Maxipen,

Semopen) is relatively resistant to gastric acid and hence can be given orally. Phenethicillin is a homologue of penicillin V (phenoxymethyl penicillin), from which it differs by the addition of a methyl group in the side chain. However, in contradistinction to potassium penicillin V, the absorption of phenethicillin from the intestinal tract is more likely to be reduced when the drug is taken with food or shortly after food has been consumed. Phenethicillin may produce higher serum levels than penicillin V, but data indicate that there is no difference, weight for weight, in their antibacterial effects on serum bactericidal testing.⁹ Therefore the drugs may be used more or less interchangeably, although phenethicillin, unlike potassium penicillin V, should be administered when the patient's stomach is empty. Peak levels in serum are attained in about one hour and persist for about four hours. Phenethicillin, like penicillin V, is inactivated by penicillinase; binding of the two drugs by serum protein is similar and amounts to 50 to 75%. Phenethicillin, like penicillin V, is used in mild to moderately severe infections and is given in a similar dosage. A dose of 125 mg., or 200,000 units, may be given at four- to eight-hour intervals, but 500 mg. or more has been given even more frequently.

Methicillin

This drug is employable against penicillin G-resistant staphylococci because methicillin (Staphicillin, Dimocillin-RT) is not appreciably inactivated by staphylococcal penicillinase and, consequently, is active against staphylococci which, *in vitro*, require more than 1.0 μ g. of penicillin G for inhibition. However, methicillin is only about a third as effective as penicillin G against susceptible organisms and, like oxacillin, cloxacillin, and nafcillin, is virtually inactive against enterococci. Occasionally, an infection that appeared susceptible on *in-vitro* testing has persisted despite optimal therapy with methicillin; but, to some extent, this has been true of all antimicrobial drugs, including the other available penicillinase-resistant penicillins.

The drug is unsuitable for oral administration and is given intravenously or intramuscularly. Serum levels reach a peak from 30 minutes to one hour after intramuscular adminis-

tration. With single intramuscular doses, serum concentrations tend to decrease rapidly and may decline below the therapeutic range after three to four hours. After intravenous injection, the initial level is higher but declines more rapidly. Nearly half the injected dose is excreted in the urine within the first six hours after administration; like the other available penicillins, methicillin is excreted chiefly via the renal tubules. Methicillin is found in bile and enters other body fluids slowly.

In patients with renal insufficiency, serum levels may persist for 10 hours or longer. In very young infants, apparently because of inadequate renal reserve, the excretion of the penicillins, including methicillin, may be delayed for days, and a correspondingly high and sustained blood concentration may be present. As is true of the other available penicillins, serum levels of methicillin are not appreciably influenced by hemodialysis. Approximately 20% of methicillin is bound to plasma proteins.

The mechanism of penicillinase-resistance of methicillin and allied drugs is not known, but presumably the side chains of these penicillins prevent the splitting of the beta-lactam ring of the 6-APA nucleus. The theory of "steric hindrance" proposes that the two methoxy groups in the side chain of methicillin disallow effective contact of the ring by the enzyme.

Strains of staphylococci isolated from patients in British hospitals have been resistant to methicillin¹⁰ and cross-resistant to some of the kindred drugs, including oxacillin,¹¹ cloxacillin,¹¹ and nafcillin.¹² There is fear that indiscriminate use of these drugs may lead to an increase in such resistant strains in this country. Not only may staphylococci emerge as being resistant to methicillin by a nonpenicillinase mechanism, but methicillin also is a powerful inducer of penicillinase production. Consequently some workers have expressed concern that widespread use of methicillin may result in an increased incidence of high penicillinase-secreting staphylococci that are resistant to all the commercially available penicillins.⁵

Methicillin is given intravenously by intermittent injection in amounts of 1 to 2 Gm. every two to six hours. Methicillin should not

be added to large quantities of infusion fluids, which are often sufficiently acid to cause inactivation over a period of several hours. A dose of 0.5 to 1 Gm. can be given intramuscularly every four to six hours; a dose of 1 Gm. can be injected intramuscularly in 1.5 to 2 ml. of distilled water.

Intrapleural and intra-articular injections of 0.5 to 1 Gm. of methicillin, dissolved in 5 to 10 ml. of sterile normal saline, have been given daily to patients with infections due to susceptible organisms. Methicillin also has been administered as an aerosol to combat selected staphylococcal infections of the lung. A dose of 0.5 Gm. of the drug can be dissolved in about 3 ml. of distilled water and inhaled during a period of about 20 minutes four times daily by use of a pump and nebulizer. Methicillin has also been used in the form of eye drops or eye ointment at a 1% concentration.

Oxacillin

This drug (Prostaphlin, Resistopen) is penicillinase-resistant but is also relatively acid-resistant; hence it can be given orally as well as parenterally. Oxacillin is much more resistant to gastric acid than is penicillin G and only somewhat less resistant than penicillin V. Although oxacillin may be slightly less resistant to penicillinase, its antistaphylococcal effect is significantly greater than that of methicillin.^{13,14} Because of the nature of its side chain, oxacillin is known as an isoxazolyl penicillin.

When oxacillin is given orally in a single dose, peak serum levels occur in different persons after intervals varying from 30 minutes to two hours. Food interferes with the absorption of oxacillin and decreases its serum levels. On oral administration of oxacillin, considerable variation in serum levels and their duration occurs in the same person, as well as among different persons, and occasionally no serum levels are demonstrable. Such erratic serum levels have considerably tempered initial enthusiasm for oral use of the drug. As a generalization, after oral administration, the serum levels of oxacillin persist for about four hours. In contradistinction to methicillin, in patients having renal insufficiency, the persistence of oxacillin in the serum may be only slightly prolonged. With intramuscular ad-

ministration, peak serum levels usually occur in 30 minutes and persist four to six hours; 0.5 Gm. given intramuscularly produces blood levels comparable to those obtained on administration of 1 Gm. by mouth. Significant accumulation of oxacillin in serum does not appear to occur with recommended doses every four hours by either the oral or the parenteral route. After intravenous administration, levels of oxacillin in blood are higher than after intramuscular injection, but decline more rapidly—that is, in less than four hours.

Oxacillin and the allied drug cloxacillin are bound to serum proteins to a greater degree (80% or more) than are other commercially available penicillins.

Oxacillin is five to eight times more effective than methicillin against pneumococci and susceptible streptococci but is not as effective as penicillin G on a milligram-for-milligram basis. Although oxacillin is not the drug of choice for the treatment of infection due to these organisms, when given in doses sufficiently large to inhibit penicillase-producing staphylococci, it may be capable of controlling pneumococcal and most streptococcal infections. Therefore, some workers believe it may be unnecessary to give penicillin G conjointly to control infections which might be due to pneumococci and most streptococci before microbiologic data are reported. However, it is advisable to use penicillin G or V in proved pneumococcal or streptococcal infections. Similar conclusions have been made regarding use of nafcillin and cloxacillin by certain investigators.

Oxacillin does not appear to be excreted well in sweat, may not diffuse readily into certain body cavities, and may not be present in substantial amounts in some body fluids. It does appear in bile, pleural and amniotic fluids, and milk. The extrarenal inactivation of oxacillin seems to be greater than that of methicillin. The higher biliary excretion of oxacillin, compared to methicillin, may account for the somewhat lower urinary recovery of oxacillin. Nafcillin and cloxacillin resemble oxacillin in that they appear in relatively high concentration in the bile.

Oxacillin is given in oral doses of 0.5 to 1 Gm. four to six times daily, preferably when

the patient has an empty stomach. The usual daily intramuscular dose also is 0.5 to 1 Gm. every four to six hours. In severe infections, oxacillin is given intravenously every two to six hours in amounts of 1 to 2 Gm. This amount of the drug can be dissolved in 10 to 20 ml. of 5% dextrose or normal saline solution and injected during a period of several minutes. As an alternative method for intravenous use, the drug can be dissolved in 100 to 200 ml. of an isotonic solution and given during a one- to two-hour period. Oxacillin is more resistant than methicillin to deterioration in solutions prepared for intravenous use.

Nafcillin

In contradistinction to the isoxazolyl penicillins, such as oxacillin, nafcillin (Unipen) has an ethoxynaphthyl side chain. On oral administration, nafcillin produces serum levels that may be somewhat lower than those attained with oxacillin, but nafcillin persists longer in the serum and may provide better penetration of tissue. Like oxacillin and cloxacillin, nafcillin is absorbed poorly from the intestines in some patients, and serum levels are higher when the patient is fasting or has had repeated doses.¹⁵ After oral administration, peak serum levels of nafcillin are attained within one to two hours; after intramuscular injection they are attained in 30 minutes. Serum binding of nafcillin amounts to about 60% and therefore is less than that with oxacillin or cloxacillin but greater than that with methicillin. Only 5 to 10% of an oral dose is excreted in the urine during the first 12 hours, but 30 to 50% of an intramuscular dose is so excreted. The concentration of nafcillin in bile may be several times that in serum. Traces of the drug can be detected in synovial fluid. Its *in-vitro* antibacterial activity exceeds that of methicillin and approximates that of oxacillin.

Despite the availability of similar drugs, continued availability of nafcillin, especially preparations of the drug for parenteral administration, appears desirable because of the concentration and persistence of nafcillin attained in the body tissues.

The oral dose of nafcillin is 0.5 to 1 Gm. every four to six hours when the patient's stomach is empty. When administered intra-

muscularly, 0.5 to 1 Gm. also is given every four to six hours. A dose of 1 to 2 Gm. is given every two to six hours intravenously in the manner previously noted for oxacillin.

Cloxacillin

Like oxacillin, cloxacillin (TegoPen) is an isoxazolyl penicillin and differs chemically from the latter only in that it has a chlorine atom in its structure. Serum levels after oral administration of cloxacillin are at least twice as high as those after oxacillin use;^{16,17} but cloxacillin is more rapidly excreted.

Indications

Unlike methicillin, cloxacillin is less effective against a large inoculum than against a small one, probably because the drug is less resistant to staphylococcal penicillinase than is methicillin. On *in-vitro* testing, cloxacillin is less active than penicillin G, five to ten times more active than methicillin, and about twice as active as oxacillin.

Dosage

After oral administration, peak serum levels of cloxacillin are usually attained in about one hour and persist four to six hours. As aforementioned, in some patients the drug is poorly absorbed from the intestines, or not at all, and serum levels are lower in the nonfasting state. Accumulation of cloxacillin in serum does not appear to occur after multiple doses. Twenty-five to 30% of a given dose is excreted in the urine within six hours, and significant amounts are excreted in the bile.

In the study of Sidell and co-workers¹⁸ on intramuscular administration, cloxacillin, oxacillin, and nafcillin were equally active when absorption, serum antistaphylococcal activity, and serum binding were combined in a single assay method.

A preparation of cloxacillin for parenteral use is not commercially available in the United States. The oral dose of cloxacillin varies from 0.25 to 1 Gm. given every four to six hours when the patient's stomach is empty.

Ampicillin

This drug is orally and parenterally ad-

ministered and has an alpha-aminobenzyl group in place of the benzyl side chain of penicillin G.

Indications

Ampicillin (Polycillin, Omnipen, Penbritin, Principen) is active against more than 80% of strains of *Escherichia coli* and against about 90% of strains of *Proteus mirabilis*; it is likewise effective against certain strains of other gram-negative bacilli such as *Haemophilus influenzae*, *H. parainfluenzae*, *Salmonella*, *Shigella*, *Brucella*, and *Bacteroides*. The drug is also active against *Neisseria*, *Clostridia*, pneumococci, and streptococci. However, it is inactive against penicillin G-resistant staphylococci, as well as against most strains of *Klebsiella-Aerobacter*, indole-producing *Proteus*, and *Pseudomonas* organisms. Ampicillin and phenethicillin are considerably more active than the other available semisynthetic penicillins against enterococci. Also, ampicillin may have an anti-enterococcal effect even greater than that of penicillin G, at least against certain strains of these microorganisms.¹⁹ Ninety per cent or more of strains of enterococci are susceptible *in vitro* to ampicillin; streptomycin or kanamycin may enhance the anti-enterococcal effects of ampicillin.

On oral administration, levels of ampicillin in serum and urine do not appear to be greatly lessened when the drug is taken with food.²⁰ After oral administration, peak levels in serum are reached in about two hours and trace levels are present for at least six hours. When the drug is given intramuscularly, peak levels in serum are achieved in 30 minutes to one hour, and the levels are considerably higher and more prolonged. Intravenous injection of ampicillin produces higher peak levels in the serum and more rapid excretion of the drug than does intramuscular administration.²¹ In patients with renal insufficiency, the duration of serum concentration of ampicillin may be half again as long as that in normal subjects. Susceptible gram-negative bacilli are inhibited by feasible levels of ampicillin in serum—that is 5 μ g. of the drug per milliliter or less. Ampicillin is bound to plasma proteins only to the extent of about 10 to 20%.

The concentration of the drug in the bile

may be 300 times that in the plasma. High concentrations of ampicillin also appear in the urine.

Although good results have been obtained in some patients with systemic infections from *Salmonella*,²¹ ampicillin has not as yet displaced chloramphenicol as the drug of choice in acute typhoid fever; there are some indications, however, that the relapse rate in typhoid fever after use of ampicillin is lower. Contrariwise, ampicillin is much more effective than chloramphenicol in eradicating the typhoid carrier state.²² Fecal or urinary excretors of *Salmonella* organisms are more likely to respond to ampicillin therapy than are biliary excretors; biliary excretors without cholelithiasis respond better than those with stones, but after cholecystectomy at least half will respond.

The drug has been effective in meningeal, respiratory, urinary, and other infections due to susceptible microorganisms. Because ampicillin is active against *H. influenzae*, meningococci, and pneumococci, it is being investigated as a single agent in the initial treatment of patients suspected of having acute bacterial meningitis before the report of definitive microbiologic data, and thus far, results are encouraging.^{23,24} Ampicillin also has been effective in cases of bronchitis and pneumonia due to *H. influenzae*. The drug has eradicated urinary infections and bacteremia due to *E. coli*, *P. mirabilis*, and enterococci. Data indicate that, in enterococcal bacteremia and endocarditis, ampicillin may approach the efficacy of combined streptomycin-penicillin G therapy.¹⁹ As aforementioned, the anti-enterococcal effect of ampicillin may be enhanced by conjoint use of streptomycin or kanamycin. Ampicillin may be preferred to the tetracyclines under certain circumstances, as in pregnant women and infants, in order to avoid tetracycline-induced adverse reactions which are likely to occur in such patients. Ampicillin also has been recommended as an alternative drug to the tetracyclines in the management of intestinal malabsorption²⁵ and in the treatment of pertussis.²⁶

Dosage

A dose of 0.5 to 1 Gm. of ampicillin is given

every four to six hours orally. It has been given parenterally in the same dosage, but higher doses are not uncommon. The stability of sodium ampicillin may decrease markedly with increases in its concentration, and the storage of injection solutions may be hazardous. Five to 25% of the initial potency of the drug may be lost within a few hours, even when solutions are stored at refrigeration temperatures. The presence of dextrose and lactate in solutions of ampicillin may further accelerate loss of the drug's potency.

A dose of 500 mg. of ampicillin dissolved in 5 to 10 ml. of sterile normal saline has been given by intrapleural and intra-articular injection. Ampicillin also has been used in the form of eye drops or eye ointment in a 1% concentration.

There are other semisynthetic penicillins that have reached the stage of preliminary clinical investigation, examples of which are dicloxacillin^{27,28} and hetacillin.²⁹

Dicloxacillin

Like oxacillin and cloxacillin, dicloxacillin is one of the isoxazolyl group of semisynthetic penicillins. Dicloxacillin differs from cloxacillin in having an additional chlorine in the side chain of the phenyl ring. The ability of dicloxacillin to resist gastric acid is similar to that of cloxacillin. There are preliminary indications that methicillin-resistant staphylococci may be inhibited by dicloxacillin; consequently, in infections due to staphylococci which resist the commercially available antistaphylococcal penicillins, dicloxacillin might have special application. On oral and parenteral administration of dicloxacillin, serum levels are twice as high as those after cloxacillin use and four times those after oxacillin use. In the fasting state, oral doses produce serum levels that persist about four hours. Serum levels after intramuscular administration of dicloxacillin may not be much higher and only slightly more prolonged than after oral administration, but are more reliable. Intravenous administration of dicloxacillin produces higher initial levels in serum than follow intramuscular injection, but the drug is eliminated more rapidly.

Preliminary studies in human staphylococcal

infections indicate that dicloxacillin is at least as effective as the commercially available drugs.

The usual oral and intramuscular dose of dicloxacillin is 0.25 to 0.5 Gm. given every four to six hours; 1 Gm. or more has been given every two to four hours intravenously.

Hetacillin

This drug is derived from an acylation condensation procedure in the synthesis of ampicillin. Hetacillin and ampicillin have similar antibacterial spectra and appear to have at least comparable potency; hetacillin is also hydrolyzed by penicillinase. When equal oral doses are given, serum levels on use of hetacillin exceed those of ampicillin after the fourth hour. When given intravenously, hetacillin is said to produce serum concentration considerably higher than that after injection of ampicillin. The renal clearance of hetacillin is similar to that of ampicillin, and the appearance in the urine of a larger proportion of the administered dose of hetacillin has been taken to indicate an even greater resistance to extrarenal destruction than is true for ampicillin. Hetacillin has been effective in bacteremia due to *E. coli*, pneumonia due to *Diplococcus pneumoniae* and *H. influenzae*, urinary infections due to susceptible gram-negative bacilli, shigellosis, and salmonellosis. It has been concluded that 6 Gm. of hetacillin per day should be therapeutically equivalent to 8 Gm. of ampicillin. It is conceivable that in the future hetacillin may be preferred to ampicillin because of the better utilization of hetacillin in human subjects.

Untoward Effects

Allergy is the major untoward effect encountered on use of the penicillins and may be present in 3 to 5% of the general population and in as many as 10% of patients who previously have been treated with the drugs. Cross-allergenicity among the natural penicillins and the semisynthetic penicillins apparently reflects the 6-APA nucleus which they have in common. It is theorized that catabolic products of the penicillins, such as penicilloyl compounds, may unite with body protein and be responsible

for some of these allergic reactions. It is also possible that a macromolecular protein or peptide residue in the penicillins is responsible for some of these reactions. This impurity may result from certain procedures in the manufacture of the drugs and may be removable by dialysis or column fractionation.^{30,31}

Oral administration of a penicillin is least likely to induce allergy, topical application is most likely, and injection is of intermediate capacity in this regard. Methods employed in attempts to identify allergic subjects include skin testing with the drugs as well as with the derivative penicilloyl-polylysine, conjunctival testing, and tests of passive transfer, serum hemagglutination, and indirect basophilic degranulation; none of these, however, is totally reliable. Persons with a history of such conditions as asthma, eczema, or hayfever are more likely to demonstrate hypersensitivity, particularly anaphylaxis, on use of the penicillins. The genesis of penicillin allergy is complicated by sources of inadvertent acceptance of the drugs, such as milk, fowl, and viral vaccines.

Desensitization may aid in avoiding further reactions to the penicillins. Such substances as antihistaminics, epinephrine, penicillinase, and corticosteroids may help in their management. However, penicillinase may also cause allergic reactions, and the enzyme would probably not be helpful in cases wherein a penicillinase-resistant drug is causative. Although corticosteroids are of use in allergic states, the presence of infection sometimes makes it hazardous to use such drugs.

It is common experience that various skin reactions, including contact dermatitis, angio-neurotic edema, glossitis, hairy tongue, stomatitis, thrush, pruritus ani and vulvae, drug fever, eosinophilia, serum sickness, and anaphylaxis, may complicate use of the penicillins. The incidence of fatality in anaphylaxis is estimated to approach 10%. More unusual reactions include purpura, pericarditis, toxic psychoses, hematemesis due to an urticaria-like reaction of the gastric mucosa, and diffuse vasculitis. Gastrointestinal irritation, including diarrhea, may occur after the use of an orally administered penicillin but is seldom severe enough to require discontinuation of therapy. Pain on intramuscular injection of the semi-

synthetic penicillins is more likely on use of ampicillin and nafcillin. Sterile abscesses rarely occur at the site of intramuscular injections of the penicillins. Chemical phlebitis on intravenous administration is most commonly associated with use of nafcillin.

In patients requiring sodium restriction, such as those with heart failure or renal dysfunction, who are receiving one of the semi-synthetic penicillins, the increased intake of sodium should be considered. In such cases, one should recall that each 4 Gm. of methicillin supplies 230 mg. or 10 mEq. of ionic sodium.

Granulopenia and anemia have occurred after administration of methicillin,³² and oxacillin and cloxacillin have caused transient leukopenia.⁵

The penicillins, when given in large amounts, may cause cortical irritation, including convulsions, especially in patients with decreased renal function. Chronic brain damage may result. Since the penicillins, in addition, have precipitated acute psychosis, and since anaphylactic reactions have also resulted in chronic brain damage,³³ perhaps one should be more aware of the potential neurotoxicity of these drugs.

It appears increasingly likely that methicillin has significant nephrotoxicity.³⁴

The significance of increased activity of serum transaminase during therapy with ampicillin, oxacillin, and cloxacillin remains unclear. Oxacillin has been accused of causing hepatic toxicity,³⁵ including cholestatic hepatitis.³⁶

Food interferes with the intestinal absorption of phenethicillin, oxacillin, cloxacillin and nafcillin, and in some cases the decreased serum levels may be therapeutically inadequate.

The penicillins may depress the coccal members of the body flora, thereby encouraging bacteremia, pneumonia, and other infections caused by overgrowth of gram-negative bacilli and *Candida*. Periodic examination of the sputum and stools may reveal changes in the body flora in time to avert clinical superinfection. In series of patients treated with methicillin, as many as a third have experienced superinfection, including fatal bacteremia, due to gram-negative bacilli. Ampicillin-induced superinfections are most frequently due to *Pseu-*

domonas and *Klebsiella-Aerobacter* organisms.

Since strains of coagulase-positive staphylococci, isolated from patients in British hospitals, have been resistant to methicillin and cross-resistant to the commercially available kindred agents, it is feared that when these drugs are used in a given area for a period of time, the incidence of such resistance may increase. This ominous possibility should be sufficient to militate against indiscriminate use of these drugs. Coagulase-negative staphylococci may be even more prone to emerge as being resistant to these drugs.

Although the effect of the penicillins on the fetus is not precisely known, as a generalization, these drugs appear to be nonteratogenic in the human.

The serum levels of all the penicillins, natural and semisynthetic, may be increased on conjoint administration of probenecid; but a number of patients are unable to tolerate this drug because of gastrointestinal irritation.³⁷ Also, side-effects of probenecid may cause confusion with those of the penicillins or with manifestations of the infection being treated. Such side-effects include dermal reactions, anaphylaxis, fever, chills, and anemia. Of course, concomitant administration of probenecid in infections of the urinary tract would not be advisable, since decreased urinary concentration of the antibiotic would be likely.

Present Status

The precise application of the individual semisynthetic penicillins cannot be currently evaluated, and problems of their evaluation undoubtedly will be increased on discovery of still newer derivatives that have possible clinical use. However, of the semisynthetic penicillins which are destroyed by penicillinase, phenethicillin is used more or less interchangeably with penicillin V but, unlike the latter, must be given when the patient's stomach is empty. Ampicillin has proved effective in such infections as influenzal meningitis, bacteremia due to *E. coli*, and systemic salmonellosis and hence has a more assured niche in the current therapeutic armamentarium.

Experiences to date make it clear that methicillin, oxacillin, and nafcillin are efficacious in the parenteral therapy of serious infections caused by penicillin G-resistant staphylococci. Also, oxacillin, cloxacillin, and nafcillin are ef-

fective on oral administration in selected infections due to these organisms. These penicillinase-resistant drugs have given cure rates as high as 70% in some series of staphylococcal bacteremia and have been effective in at least 50% of cases of staphylococcal endocarditis. Many other staphylococcal infections (including pulmonary, skeletal, dermal, and urinary) have been eradicated by these drugs.

Despite their achievements, the overall mortality rate after use of these drugs in patients with severe staphylococcal infections is between 30 and 40%. This rate appears to largely reflect factors in the host responsible for the susceptibility to, as well as the severity of, the infection. In severe staphylococcal infections, such as endocarditis, doses of 8 to 24 Gm./per day or greater are usually necessary for cure; treatment of endocarditis is continued for at least three to four weeks.

The effectiveness of a penicillinase-resistant penicillin depends on at least two properties: (1) its inherent antistaphylococcal potency, and (2) its degree of resistance to penicillinase. The ultimate clinical application of a given drug will be influenced by other factors, including its comparative toxicity on long-term observation.

Of available data on the antistaphylococcal semisynthetic penicillins, the following are noteworthy: They should be used only in selected infections known to be, or highly suspected of being, due to penicillin G-resistant staphylococci; they should not be used in patients allergic to other penicillins; and they should be used cautiously in patients with other allergies, particularly asthma. Higher serum levels of these drugs are required than is necessary with penicillin G, since the agents are less bactericidal than is penicillin G, weight for weight, *in vitro*. However, since the minimal inhibitory concentrations of oxacillin, cloxacillin, and nafcillin³⁸ against pneumococci and streptococci, excepting enterococci, approach those of penicillin G, some workers, at least as an investigational procedure, give one of these drugs as a single agent in infections in which either staphylococci or one of the aforementioned cocci is possibly causative, until microbiologic data are available. In other words, conjoint use of penicillin G or V, theoretically, may be unnecessary under such circumstances;

when the pathogen and its *in-vitro* susceptibilities are known, one switches to a natural penicillin or continues the penicillinase-resistant penicillin, accordingly. This generalization, if supported by further investigation, may be particularly applicable to hospital infections, possibly due to staphylococci.

Discriminate use of the semisynthetic anti-staphylococcal penicillins may help minimize the emergence of resistant bacterial strains and also aid in reducing the problem of allergy to the penicillins.

Because bacterial endocarditis is a potential complication of open-heart surgery, especially when intracardiac prostheses are used, the prophylactic administration of a penicillinase-resistant penicillin to such patients is being investigated. Although delayed infection may sometimes occur from exogenous sources, in most cases it appears to reflect contamination at surgery. Administration of such a drug for 12 to 24 hours before operation and no longer than 72 hours afterward is recommended by some workers in order to avoid undue disturbance of the normal microflora and consequent enhancement of superinfection by resistant organisms on the valve or elsewhere in the body. Conjoint administration of streptomycin is generally not advised, since there is little evidence that an enhanced antibacterial effect is usually achieved thereby, and the likelihood of streptomycin-susceptible gram-negative bacillary infection is remote. Of course, use of a penicillinase-resistant penicillin in this manner will not protect against naturally resistant strains of coagulase-positive staphylococci. Of greater theoretic concern is the finding that coagulase-negative strains appear even more likely to emerge as being resistant to such drugs, and these staphylococci are not an uncommon cause of postcardiotomy endocarditis. It has been theorized that simultaneous use of another antistaphylococcal drug, such as cephalothin, would give broader coverage against resistant staphylococci; but, contrariwise, cephalothin by its conjoint effect on the microflora might further enhance the incidence of postoperative infection due to such organisms as *Candida*. Prophylactic use of a penicillinase-resistant penicillin is also being investigated by some workers in selected neuro-

surgical, orthopedic, and dental procedures.

Oxacillin, cloxacillin, and nafcillin are more active, weight for weight, than methicillin, and consequently the question has been raised whether the continued availability of methicillin is necessary. Also, use of oxacillin may be associated with less likelihood of nephrotoxicity, hematotoxicity, and superinfection than is true with methicillin therapy. However, on comparison with methicillin, oxacillin does not appear to be excreted well in sweat, may not diffuse readily into certain body cavities, and may not be present in substantial amounts in some body fluids; also oxacillin may be hepatotoxic. In this same regard, it is conceivable that oxacillin in turn may be replaceable with cloxacillin because the latter is more active and provides higher and more predictable blood levels. Nafcillin continues to be preferred in certain situations because of its more persistent levels in serum and especially in tissues.

If one supports the concept that the extent of a drug's binding to body protein indicates its ability to inhibit bacterial growth, or the lack of it, one should recall that dicloxacillin, cloxacillin, and oxacillin are highly bound, nafcillin is bound to an intermediate degree, whereas methicillin is least bound. Although some workers have indicated that a drug highly bound to protein may be less available for bacterial inhibition, it is also conceivable that this depot-effect may prolong the drug's antibacterial action.

Summary

Of the commercially available semisynthetic drugs, phenethicillin is used more or less interchangeably with penicillin V. Oxacillin, cloxacillin, and nafcillin are more active weight by weight than methicillin, can be given orally as well as parenterally, and are effective anti-staphylococcal agents. Serum levels of cloxacillin may be twice as high as those of oxacillin. Nafcillin is sometimes preferred because its level persists longer in serum and tissue. Ampicillin has been effective in such gram-negative bacillary infections as influenzal meningitis and bacteremia due to *E. coli*. Long-term evaluation is required to assess the comparative worth of new antibiotics, because

the benefits as well as the untoward effects of a drug may not become known until several years have elapsed after its clinical availability. The increasing number of effective penicillin derivatives and the diversity of their clinical

application, as well as their potential untoward effects, make it incumbent on the practitioner to be familiar with these drugs and to utilize them in a selective manner.

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References

1. Martin, W. J.: Antibacterial Therapy. I. Newer Agents Effective Against Penicillin G-Resistant Staphylococci: Newer Semi-synthetic Penicillins. *Minnesota Med* 47:577, 1964.
2. Martin, W. J.: Newer Antimicrobial Agents Having Current or Potential Clinical Application. *Med Clin N Amer* 48:255, 1964.
3. Martin, W. J.: Newer Penicillins. *Med Clin N Amer* 51:1107, 1967.
4. Hewitt, W. L.: The Penicillins: A Review of Strategy and Tactics. *JAMA* 185:264, 1963.
5. American Medical Association, Council on Drugs: New Drugs. Chicago, American Medical Association, 590 pp, 1967.
6. Martin, W. J., and Wellman, W. E.: Clinical Use of Antimicrobial Agents. In Brennemann, J., and Kelly, V. C.: *Practice of Pediatrics*. Hagerstown, Maryland, W. F. Prior Company, vol. 1, pt. 2, pp. 1-43, 1963.
7. Martin, W. J., and Wellman, W. E.: Clinically Useful Antimicrobial Agents. I. General Considerations. *Postgrad Med* 33:105, 1963.
8. Hamilton-Miller, J. M. T.: Penicillinacylase. *Bact Rev* 30:761, 1966.
9. Martin, W. J., and Nichols, D. R.: Penicillin V and Phenethicillin Potassium in Serum: Comparison of Concentrations and of Antibacterial Effects. *Proc Staff Meet Mayo Clin* 35:577, 1960.
10. Colley, E. W., McNicol, M. W., and Bracken, P. M.: Methicillin-Resistant Staphylococci in a General Hospital. *Lancet* 1:595, 1965.
11. Barber, Mary, and Waterworth, Pamela M.: Antibacterial Activity of the Penicillins. *Brit Med J* 1:1159, 1962.
12. Rosenman, S. B., and Warren, G. H.: Comparative *In Vitro* Activity of Semi-synthetic Penicillins Nafcillin and Oxacillin. In Sylvester, J. C.: *Antimicrobial Agents and Chemotherapy—1962*. Proceedings of the Second Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, October 31-November 2, 1962. Ann Arbor, Michigan, American Society for Microbiology, pp. 369-378, 1963.
13. Kirby, W. M. M., Rosenfeld, Lona S., and Brodie, Jean: Oxacillin: Laboratory and Clinical Evaluation. *JAMA* 181:739, 1962.
14. Simon, H. J., and Rantz, L. A.: The Newer Penicillins. II. Clinical Experiences With Methicillin and Oxacillin. *Ann Intern Med* 57:344, 1962.
15. Klein, J. O., and Finland, M.: Nafcillin: Antibacterial Action *In Vitro* and Absorption and Excretion in Normal Young Men. *Amer J Med Sci* 246: 10, 1963.
16. Kislak, J. W., Eickhoff, T. C., and Finland, M.: Cloxacillin: Activity *In Vitro*, and Absorption and Urinary Excretion in Normal Young Men. *Amer J Med Sci* 249:636, 1965.
17. Turck, M., Ronald, A., and Petersdorf, R. G.: Clinical Studies With Cloxacillin: A New Antibiotic. *JAMA* 192:961, 1965.

18-38 May be secured from the author or the reprints.

President's Letter

Continued from Page 1777.

I also want to take this opportunity to thank the entire office force of the State Medical Association for their untiring (and many times very tiring) efforts to make our great Organization click. My own personal thanks go especially to Harold Brunn, our outstanding executive secretary, to his girls—Fitz, Marcy, and the rest, as well as to my own chief critic and advisor, Elaine Nye, the Girl Friday to our tremendous Editor-in-Chief, Dr. Carl O. Rice. Few ever get to know of the enormous amount of work which Dr. Rice and his Board of Editors do to make this MINNESOTA MEDICINE of ours one of the outstanding medical journals in the country. I salute all of you!!!

I further wish to extend a world of thanks

and credit to all of our very active Committees. It has been my privilege to attend many Committee meetings; I apologize for not having been able to get to all of them, but time simply would not permit. Our system of checks and balances within the Association will continue to serve us well over a long period of time. No Committee or President can ever get very far out of line!!!

Now, may I wish all of you a Blessed Christmas and a wonderful 1968!!!



C. G. Sheppard, M.D.
President

Minnesota State Medical Association



Abstracts, Briefs and Commentaries

THE MANAGEMENT OF ERYTHROBLASTOSIS FOETALIS MANITOBA—1967

The pathogenesis of erythroblastosis fetalis is reviewed. Of the affected infants approximately 45 to 50% do not require treatment and an additional 25 to 30% should survive and kernicterus be avoided with exchange transfusions. Approximately 20 to 25% of infants will be stillborn or hydropic before term and will require early delivery and, in some cases, intraperitoneal fetal transfusion. Spectrophotometric examination of amniotic fluid has increased the accuracy of ante-natal prediction of severity of fetal affectation from 60 to 95%. In the past five years 749 amniotic fluid studies were performed on 402 sensitized women. Twenty (5%) predictions were inaccurate and only eight (2%) were so inaccurate that the fetus was in jeopardy. Amniocentesis was without significant complications, although a few cases were encountered in which it was suspected that the severity of the fetal disease was increased by the associated passage of fetal erythrocytes into the mother's circulation. In view of the possible risk, amniocentesis is restricted to those patients who have definite risk of fetal death, or about 50% of isoimmunized pregnancies.

In Manitoba 8% of all fetuses with erythroblastosis fetalis would have been stillborn or hydropic before 32 weeks gestation. Intraperitoneal transfusion of the fetus was carried out 128 times in 61 fetuses in the past three years. Twenty-four infants (43%) were salvaged. The salvage rate was 58% if hydropic infants were excluded. In the past 16 months, due to increased experience, these values have increased to 68% and 83%, respectively. The risk of fetal death due to the trauma of the procedure has fallen from 19 to 7%.

The perinatal mortality rate due to erythroblastosis fetalis in the province of Manitoba for the year ending October 31, 1966, was 10.1%; 14 to 138 affected infants died. Four of these deaths were preventable using accepted methods of evaluation and treatment. Five other deaths were probably preventable, as amniotic fluid studies were not obtained or errors were made in management. Four perinatal deaths were not preventable. Optimum management would have resulted in a perinatal mortality rate of 3.6%. This goal is possible only if patients are aware of the need for good prenatal

care and physicians obtain the indicated prenatal antibody tests. Amniotic fluid studies, early delivery and intraperitoneal fetal transfusions may be indicated. The danger of jaundice early in the newborn period must be appreciated. In addition to blood grouping and antibody determinations at the first prenatal visit, the Rh positive woman with no "atypical" antibodies should have blood checked again at 32 to 36 weeks gestation. The unsensitized Rh negative woman should have monthly antibody tests during pregnancy and six weeks post partum. Women with antibodies of any kind should have monthly blood tests until 24 to 26 weeks gestation and then twice monthly and six weeks post partum. Passive administration of Rh immune gamma globulin to Rh negative women without Rh antibodies immediately after delivery of an Rh positive infant shows great promise as a means to prevent Rh isoimmunization. In the near future amniocentesis, early delivery, intraperitoneal fetal transfusion and exchange transfusion may be unnecessary.

Leon L. Adcock, M.D.
Minneapolis, Minnesota

Bowman, John M.: The Management of Erythroblastoses Foetalis-Manitoba, 1967. Manitoba Medical Review, 1967.

IMMEDIATE SURGERY FOR CARDIAC AND GREAT VESSEL WOUNDS

Thirteen patients were treated for wounds of the great vessels or heart. Ten who were treated by surgical exploration and repair survived. Of three treated conservatively (i.e., by pericardiocentesis, tube thoracotomy, etc.), one died. Delay in diagnosis and in definite surgery after diagnosis were two significant errors in management. The simplest, safest, and most effective management of these wounds is immediate thoracotomy and specific therapy. The authors' opinion is contrary to opinions expressed by others who advocate the conservative approach.

Jerome T. Grismer, M.D.
Minneapolis, Minnesota

Sauer, P. E. and Murdock, C. E., Jr.: Immediate Surgery for Cardiac and Great Vessel Wounds. Arch Surg 95:7, 1967.

A HICCUP REMEDY THAT WORKS

Believe it or not, there's a hiccup remedy that almost always works—but should be used only by physicians.

It involves inserting a flexible tube into a nostril and stimulating nerves in the pharynx, the area at the back of the mouth where nasal passages join the throat.

The process worked in 84 of 85 cases, report three physicians at the University of Chicago School of Medicine and a fourth colleague on the faculty of medicine at Cairo University, United Arab Republic.

Hiccups can be troublesome or even dangerous during surgery. These involuntary contractions of the diaphragm have a variety of causes; and the attempted medical remedies have been almost as numerous as those which come from folklore.

Physicians, too, have tried such remedies as swallowing ice, holding the tongue, frightening with a loud noise, and pressing on the eyeballs. Their results have been about as unpredictable as those of laymen. On a more sophisticated level, they have tried drugs and nerve blockage, often with similar results.

Hiccups seem to occur frequently during light anesthesia. One remedy has been to deepen the anesthesia; however, several times more anesthetic is required to stop hiccups than merely to induce unconsciousness. In some cases, this is undesirable.

Hiccups stopped immediately in 64 anesthetized and 20 conscious persons, the report said, when pharyngeal nerves were stimulated by jerky, back-and-forth movements of the tubing. Patients ranged in age from 18 months to 73 years.

In ten cases, a variety of drugs had failed to stop hiccups, but they ceased almost immediately with the new method, according to the authors. In five cases, the hiccups returned, but stopped during retreatment. Only one anesthetized patient failed to respond to treatment.

A caution should be repeated, however: inserting a tube or other object deeply into nasal passages can be dangerous and should be done only by a physician. Do not attempt this remedy yourself.

The reasons some harmless "home remedies" are sometimes successful—such as swallowing ice or water—may be that they, too, result in stimulation of the pharyngeal nerves, the report points out.

American Medical Association

Salem, M. Ramez, Rattenborg, Christen C., Holaday, Duncan A., and Baranka, Anis: Pharyngeal Stimulation. *JAMA*, October 2, 1967.

ARTERIAL EMBOLISM—SURGICAL TREATMENT AND RESULTS

Seventy-eight patients underwent surgical treatment for 81 emboli. Myocardial infarction and mitral valve disease with atrial fibrillation was the predominant source. The incidence of excellent results was twice as high if operation were performed before rather than after 12 hours. Conversely, the poor results were almost four times greater if operation was delayed longer than 12 hours. The authors describe their method of localization and removal of the emboli.

Jerome T. Grismer, M.D.
Minneapolis, Minnesota

Billig, D. M., Hallman, G. L., and Cooley, D. A.: Arterial Embolism—Surgical Treatment and Results. *Arch Surg* 95:1, 1967.

PREGNANCY AND HIGH ALTITUDE

Women should stay below the altitude of 10,000 feet in the last three months of pregnancy, advises a Denver physician in the *Journal of the American Medical Association*. The unborn child may be damaged by lack of oxygen if his mother exceeds this altitude in the mountains or in an unpressurized airplane. Skeletal deformities, lack of teeth and hair, brain impairment, and occasionally even death of the fetus have been attributed to lack of oxygen.

"I recommend that women who are pregnant and in the last trimester stay below 10,000 feet in the mountains and that they do not travel in an unpressurized plane while in mountain country. Women in the last three months of pregnancy who are traveling at altitudes over 10,000 feet should breathe supplemental oxygen to protect the fetus if the plane is not pressurized and if travel in an unpressurized plane cannot be avoided," Dr. E. Stewart Taylor wrote.

Most large, commercial planes are pressurized and thus provide the necessary oxygen. A woman in the last three months of pregnancy should consult her physician before flying, however.

American Medical Association

AUGMENTATION OF ARTERIAL COLLATERAL BLOOD FLOW

In dog experimentation and computer analysis, the collateral flow into the hind extremities was analyzed with six agents being tested as to their ability to increase the micro-circulatory flow.

Of the agents (heparin and blood volume, plasma, saline, dextran 75 and dextran 40), the best results followed the administration of dextran 40. This seems primarily related to lowering of blood viscosity. The mechanism is still obscure.

Jerome T. Grismer, M.D.
Minneapolis, Minnesota

Moraes, I., Texeira, E., Arbit, J., and Bergan, J. J.: Augmentation of Arterial Collateral Blood Flow. Arch Surg 95:49, 1967.

A TEN-YEAR EXPERIENCE WITH URETEROILEOSTOMY

One-hundred-ten cases of ureteroileostomy are reviewed with special emphasis on mortality and complications. In sixty-four instances this means of urinary diversion was used to treat a malignant condition; of these, forty-eight patients had carcinoma of the bladder. Ureteroileostomy was employed forty-six times for "benign" conditions, including thirty-three cases of neurogenic bladder dysfunction. Only forty percent of the entire group had an uncomplicated postoperative course. Sixty-four of the procedures done in patients with malignant disease had at least one complication and early postoperative complications were more frequent in this group. There were seven deaths in this group of cases compared to only one death after ureteroileostomy done for a so-called benign condition. Only two ureteroileal leaks occurred in this series and both patients were operated for malignant disease. Eleven of fourteen wound dehiscences occurred in the malignant group and six of eight wound infections. The authors comment particularly on the increased incidence of postoperative complications in those patients who have received preoperative irradiation. It is also of interest that in this series of cases there was only one instance of hyperchloremic acidosis and this was associated with an excessively long ileal loop.

Comment: To those of us who have struggled with these problems, an enlightening and inspiring report.

John Thomas, M.D.
Duluth, Minnesota

Cohen, Sidney M., and Persky, Lester: A Ten-Year Experience with Ureteroileostomy. Arch Surg 95:278, 1967.

Life

The first forty years of life give us the text; the next thirty supply the commentary.—Arthur Schopenhauer

Truth is not only violated by falsehood; it may be equally outraged by silence.
—Amiel

The world is full of willing people: some willing to work, the rest willing to let them.—Frost



Book Reviews

Be as careful of the books you read, as of the company you keep; for your habits and character will be as much influenced by the former as by the latter.

SURGERY OF RHEUMATOID ARTHRITIS—Leonard Marmor, M.D., Copyright 1967 by Lea & Febiger, Philadelphia.

During the last few years the orthopedic surgeon has become increasingly involved in the care of the rheumatoid arthritis patient. The old saw of not operating until the disease "burns itself out" is no longer applicable and surgery is now being done in all stages of disease activity. This book represents the personal views of one surgeon who has become especially interested in the rheumatoid patient. Dr. Marmor begins by emphasizing the need of cooperation between the surgeon and internist or rheumatologist, and also the frequent need of other disciplines such as physical therapy, occupational therapy, etc. Much useful information is presented throughout the book, but significant shortcomings exist in the presentation.

The chapter on knee surgery caused the reviewer to raise his eyebrows. It begins with a table listing all of the knee synovectomies the author has done. Of the 34 patients listed only one had any postoperative pain and none had any postoperative swelling of the knee! The longest follow-up is three years, and most of the patients were followed for less than one year. The author's indications for knee surgery are "persistent pain and swelling of the joint or x-ray evidence of joint involvement." This would qualify the vast majority of rheumatoid patients with knee involvement. The author uses a medial and lateral approach for the knee synovectomy, and he states that it is not necessary to remove the synovium from the suprapatellar pouch.

The chapter on hand surgery is well done with respect to technical detail, and the description of soft-tissue (tendon and tendon sheath) involvement is very clear. The author quotes Platt's statement that "the long term results are far too uncertain to justify any pressure being exerted" in urging surgery on one's patient. However, the author speaks quite strongly for the case of surgical intervention. Again Dr. Marmor makes the surprising statement of having had only one recurrence of local disease in 185 operations of synovectomy of fingers. The chapter on hip surgery is largely a discussion of the technique of arthroplasty. The author dismisses the use of femoral head prosthesis as having essentially no place in rheumatoid arthritis of the hip. The chapter on ankle involvement emphasizes tenosynovitis and extra-

articular lesions. The chapter on the foot gives proper emphasis to the Clayton procedure which involves radical resection of the metatarsal-phalangeal joints for forefoot involvement.

All in all the book serves to draw attention to an increasingly important area of surgery. I do not believe the average orthopedic surgeon will want to accept the opinions expressed here as final, but he will use this book as a good starting place to begin his exploration into a growing field of newer help for the rheumatoid arthritic patient.

Paul J. Bilka, M.D.
Minneapolis, Minn.

BIRTH CONTROL AND CONSCIENCE—M. H. Mothersill, M.D.

If conscience is to be effective, it ought to be taught to a child in the early years of life.

To be both wanted and needed ought to be the birthright of every child.

There is too much pity on the part of certain legalistic Christians for the newly fertilized ovum.

Over-population is like a disease; it becomes a vicious cycle. The opponents of birth control are opposed to war but, by their pronatalism, they produce the conditions which make war inevitable.

Twentieth Century Pharisees continue to criticize the use of abortion.

The situation in Japan was such that without abortion the Japanese could not have made the surprising success which they have accomplished.

Many of us would rather be ruined by praise than be saved by criticism.

M. H. Mothersill, M.D.
Indianapolis, Indiana

A TEXTBOOK FOR MEDICAL ASSISTANTS—By Lawton-Foy. 463 pages. Price: \$8.85. Publisher: Mosby, St. Louis, 1967.

For the medical assistant, nurse or secretary who wishes to improve her value to her employer and increase her knowledge, this book is invaluable.

It deals in two parts, first with Business Practices, and second with Clinical Practices, and includes a wide variety of problems that are pertinent in the physician's office.

Carl O. Rice, M.D.
Minneapolis, Minnesota

If it doesn't work in a week, forget it.

Contraindications: Edema; danger of cardiac decompensation; history or symptoms of peptic ulcer; renal, hepatic or cardiac damage; history of drug allergy; history of blood dyscrasia. The drug should not be given when the patient is senile or when other potent drugs are given concurrently. Large doses of Butazolidin alka are contraindicated in glaucoma.

Warning: If coumarin-type anticoagulants are given simultaneously, watch for excessive increase in prothrombin time. Instances of severe bleeding have occurred. Pyrazole compounds may potentiate the pharmacologic action of sulfonylurea, sulfonamide-type agents and insulin. Carefully observe patients receiving such therapy. Use with great caution in the first trimester of pregnancy.

Precautions: Before prescribing, carefully select patients, avoiding those responsive to routine measures as well as contraindicated patients. Obtain a detailed history and a complete physical and laboratory examination, including a blood count. The patient should not exceed recommended dosage, should be closely supervised and should be warned to discontinue the drug and re-

port immediately if fever, sore throat, or mouth lesions (symptoms of blood dyscrasia); sudden weight gain (water retention); skin reactions; black or tarry stools or other evidence of intestinal hemorrhage occur. Make regular blood counts. Discontinue the drug immediately and institute countermeasures if the white count changes significantly, granulocytes decrease, or immature forms appear. Use greater care in the elderly and in hypertensives.

Adverse Reactions: The most common are nausea, edema and drug rash. Swelling of the ankles or face may be minimized by withholding dietary salt, reduction in dosage or use of diuretics. In elderly patients and in those with hypertension the drug should be discontinued with the appearance of edema. The drug has been associated with peptic ulcer and may reactivate a latent peptic ulcer. The patient should be instructed to take doses immediately before or after meals or with milk to minimize gastric upset. Mild drug rashes frequently subside with reduction of dosage. However, rash accompanied by fever or other systemic reactions usually requires withholding medication. Purpuric rash has also been reported. Agranulocytosis, ex-

In rheumatoid arthritis, Butazolidin alka needs only a week's trial. If it doesn't work in a week, forget it.

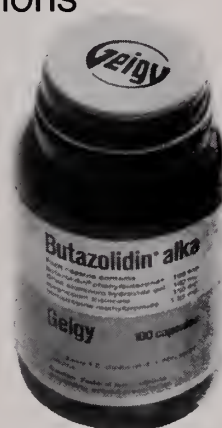
A short trial period may spare patients weeks of discomfort. That's one reason why Butazolidin alka seems a good choice when aspirin fails.

It's not for every patient. Check carefully the Contraindications, Warning, and Precautions shown below.

And adverse reactions may occur. The most common are nausea, edema and rash. Rarely, agranulocytosis has been reported. All adverse reactions are listed below, too.

You'll know quickly if it works.

And most of the time, it will.



foliative dermatitis, Stevens-Johnson syndrome, or a generalized allergic reaction similar to serum sickness may occur and require permanent withdrawal of medication. Stomatitis, salivary gland enlargement, vomiting, vertigo and languor may occur. Leukemia and leukemoid reactions have been reported. While not definitely attributable to the drug, a causal relationship cannot be excluded. Thrombocytopenic purpura and aplastic anemia may occur. Confusional states, agitation, headache, blurred vision, optic neuritis and transient hearing loss have been reported, as have hyperglycemia, hepatitis, jaundice, and several cases of anuria and hematuria. With long-term use, reversible thyroid hyperplasia may occur infrequently. Moderate lowering of the red cell count due to hemodilution may occur.

Dosage in Rheumatoid Arthritis: Initial: 3 to 6 capsules or tablets daily in 3 or 4 equal doses. Trial period: 1 week. Maintenance dosage should not exceed 4 capsules or tablets daily; response is often achieved with 1 or 2 capsules or tablets daily. 6509-V(B)R2

For complete details, please see full prescribing information.

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Also available: Butazolidin®, phenylbutazone: Tablets of 100 mg.



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*"When I couldn't even smell corned beef and cabbage,
I decided it was time for you, Doc."*



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of The Reader's Digest

2468

Law and Medicine

Background and Meaning of the McNaghten Case in the Law of Criminal Responsibility

EXONERATION OF CRIMINAL responsibility by reason of insanity is an established social phenomenon taken for granted in Anglo-American law. Debates now rage as to the relative merits of rules which attempt to spell out for judge and jury as precisely as possible when a defendant is to be punished as a criminal and when he is to be held not accountable for proscribed behavior.

There is much opinion as to the scope of testimony of experts such as psychologists and psychiatrists.

It is taken for granted that juries will rely upon the testimony of psychologists and psychiatrists in determining criminal responsibility. This practice and its underlying notions of criminal responsibility have their origin in English common law.

Criminal Responsibility

In general, one was not culpable without the will to commit an offense.¹

In English law² lack of or defective will took four forms.

Subjection to Others

Subjection to the power of others includes the commission of crime prompted by actual force and present fear of death.

Ignorance

Ignorance denotes not ignorance of the law (which one is presumed to know) but only mistake of fact, e.g., intention to kill a thief or housebreaker in one's own home but mistakenly killing a member of one's family.

Infancy

So far as infants were concerned the full age of man or woman by the law of England was 21 years. Under this age a person was termed an infant and exempted from punishment in some cases of misdemeanors and non-capital offenses. Below the age of seven years an infant could not even be punished for a capital offense. Between the ages of seven and 14 years an infant was presumed "to be unacquainted with guilt; yet this presumption will diminish with the advance of the offender's years, and will depend upon the particular facts and circumstances of his case. The evidence of malice, however, which is to supply age, should be strong and clear beyond all doubt and contradiction; but if it appears to the court and jury that the offender . . . could discern between good and evil, he may be convicted and suffer death."² Thus an infant between eight and nine years old was indicted and found guilty of burning two barns and was executed because "it appeared upon examination that he had malice, revenge, craft, and cunning."³

In the case of a nine-year-old who confessed killing a child of the same age it was found that he had hidden the blood and the body. The justices "held that he ought to be hanged; but they respited the execution that he might have a pardon." A child of ten who had killed his companion and hidden himself was actually hanged "upon the ground that it appeared by his hiding that he could discern between good and evil." A girl of 13 was burned for killing her mistress.⁴

Similarly a boy of ten was convicted of murdering a girl about five years of age and

¹Dean's case, 1 Hall 25.³

sentenced to death; although ultimately pardoned, conviction was recommended as a means of deterring other children from like offenses.⁵

Felonies Pardonable for Madness

In 1310 Parliament made felonies pardonable "for madness."⁶ This appears to be the origin of the verdict of *guilty but insane*, a verdict which did not result in acquittal but only granted the right to pardon.

An early pronouncement⁷ of the inclination to set apart a class of defendants not liable to criminal sanction is that of William Lombard of Lincoln's Inn in 1582, which states that criminal responsibility requires a guilty, comprehending mind:

"If a man or a natural fool, or a lunatic in the time of his lunacy, or a child who apparently has no knowledge of good or evil do kill a man, this is no felonious act*** for they cannot be said to have any understanding will."

In *King v. Arnold*⁸ in 1724 the court's charge to the jury was rather stringent:

". . . (N)ot every kind of partial insanity would excuse him, but it must be such a deprivation of reason as made a man no more than a brute or an infant."

In *King v. Lord Ferrers*,⁹ however, the judge charged the jury that it was:

". . . not necessary to have a complete possession of reason but a sufficient degree to comprehend the nature of the action and to discriminate between moral good and evil . . . (and the jury was charged to determine whether defendant was) guilty, judging from his capacity at the moment when he committed the act."

Ferrers plainly repudiated the statement of Coke that "it must be an absolute madness" to excuse treason. On the other hand it accorded with the statement of Hale that the jury was to ". . . judge as in the case of an infant whether there was the power of distinguishing right from wrong."¹⁰

The Lord Ferrers Case

In the case of Lord Ferrers the defendant was found guilty and executed on the ground that the murder was deliberate and that it appeared that when he committed the crime he had sufficient capacity to form a design and know its consequences. The prosecution urged that complete possession of reason was unnecessary to warrant the judgement of the law and that it was sufficient if the party had such

possession of reason as enabled him to comprehend the nature of his actions and discriminate between moral good and evil.¹¹

Lord Ferrers was tried before the House of Lords for the murder of his steward. "It was proved that he was occasionally insane and fancied his steward to be in the interest of certain supposed enemies. The steward being in the parlor with him, he ordered him to go down on his knees, and shot him with a pistol, and then directed his servants to put him to bed. He afterwards sent for a surgeon, but declared he was not sorry, and that it was a premeditated act; and he would have dragged the steward out of bed, had he not confessed himself the villain. Many witnesses stated that they considered him insane, and it appeared that several of his *relations* had been confined as lunatics. It was contended for the prosecution, that the complete possession of reason was not necessary in order to render a man answerable for his act; it was sufficient if he could discriminate between good and evil. The peers unanimously found his lordship guilty."³

Arnold's Case

In Arnold's case the jury found a prisoner guilty of maliciously shooting at Lord Onslow although "it appeared clearly that the prisoner was, to a certain extent, deranged, and that he had greatly misconceived the conduct of Lord Onslow; but it also appeared that he had formed a regular design, and prepared the proper means for carrying it into effect." Here the jury was charged that to exempt a man from punishment it must be shown that he is totally deprived of his understanding and memory and does not know what he is doing any more than an infant, a brute or a wild beast. (At the victim's request, the defendant was reprieved. He was confined to prison until his death 30 years later.)

The Hadfield Case

A brain-damaged war veteran named Hadfield was indicted for treason.¹² He was charged with firing a pistol at George III in Drurylane Theatre on May 15, 1800. On June 18 the defendant brought habeus corpus, averring poverty and requesting assignment

of counsel.* He pleaded not guilty and was remanded** for trial, which commenced on June 26.

In his opening address¹⁰ the Attorney General anticipated the defense of insanity. He stated the law as he knew it:

"If a man be completely deranged, so that he knows not what he does, if he be so lost to all sense that he cannot distinguish good from evil, and cannot judge the consequences of his actions . . . then . . . he cannot be guilty of any crime, because the will which, to a certain extent, is the essence of every crime, is wanting . . ."

The Attorney General cited three exemptions to the foregoing: idiocy, where the defendant cannot discover right from wrong; infancy, where the defendant has not attained the faculty of making such discovery; "temporary frenzy," for example, fever where the defendant cannot comprehend the consequences of his action. He went on to state that the jury was to decide on the state of mind for idiots and children, the latter not to be judged on years alone. The Attorney General also cited Coke, Hale, *King v. Arnold* and *King v. Lord Ferrers*, mentioned above. He admitted that the defendant was "discharged from the military because of mental derangement" but urged that the details of preparation for the commission of the crime showed "thought, design and contrivance in all he did."

Further in support of the last assertion the Crown produced testimony that the defendant had been asked why he made the attempt on the life of the King. The reply was that "he was tired of life and he thought he would certainly be killed if he made an attack on His Majesty's life." It was testified that after the attempt the "defendant seemed perfectly collected." There are repeated references to the defendant's perfect composure and understanding in the testimony of the witnesses for the prosecution.

Medical Testimony on Head Injury

Defense counsel Erskine agreed with the law as stated by the Attorney General but

*One of his assigned counsel, Erskine, already a busy and respected barrister, was later to become one of the most famous trial lawyers in the history of the English bar.

**See Test Your Word Score Page 1823.

stated that in his opinion: "At the moment the fatal catastrophe took place, this unfortunate man did not possess that reason which alone enables a man to distinguish between right and wrong . . ." There was extensive evidence by a surgeon and also by a physician testifying for the defense. To head wounds suffered years previously in battle they attributed recurrent outbursts of the defendant's unreasonable suspicion, gross delusions and uncontrollable violence. A fellow soldier and the defendant's wife both gave evidence of the defendant's grandiose delusions.

The prosecution was surprised by this evidence and agreed readily to the Court's strong suggestion that the defendant be acquitted. The result was essentially a directed verdict for the defendant.

That the prosecution should anticipate the defense of insanity in *Hadfield* is a clear expression of notions of criminal responsibility which are now taken for granted. The second striking feature of this case is the use by the defense of medical experts on the subject of the defendant's sanity.

The Bowler Case

Bowler was tried at the old Bailey in 1812 for shooting at and wounding another. Two weeks earlier he had been found insane by a Commission of Lunacy. There was evidence that following a seizure about one year prior to his trial he had shown "a great alteration in his conduct and demeanor; that he would frequently rise at 9 o'clock in the morning, eat his meat almost raw, and lie on the grass exposed to the rain; and that his spirits were so dejected that it was necessary to watch him, lest he should destroy himself." The jury was charged that it should convict if it found that when he committed the offense he was capable of distinguishing right from wrong and not under the influence of such an illusion as disabled him from discerning that he was doing a wrong act. The jury's verdict was guilty.¹³

The Parker Case—Aiding King's Enemies

Parker's case concerned indictment in 1812 for aiding the king's enemies by entering into the French service in time of war between France and England. The jury convicted after

being urged by the Attorney General that in order to acquit the jury must be satisfied that at the time the crime was committed the prisoner did not really know right from wrong.¹⁴

Bellingham's Case—Gratifying Revenge

In Bellingham's case the jury convicted on the judge's charge that in order to support the defense of insanity it ought to be proved by the most distinct and unquestionable evidence that the prisoner was incapable of judging between right and wrong, that in fact it must be proved beyond all doubt that at the time he committed the act he did not consider that murder was a crime against the laws of God and nature, that there was no other proof of insanity which would excuse murder or any other crime. The trial judge further charged "that in the species of insanity in which the patient fancies the existence of injury and seeks an opportunity of gratifying revenge by some hostile act, if such person be capable in other respects of distinguishing between right and wrong, there would be no excuse for any act of atrocity which he might commit under this description of derangement."¹⁵

"The above direction does not appear to make a sufficient allowance for the incapacity of judging between right and wrong upon the very matter in question, as in all cases of monomania," Roscoe comments on this charge.¹⁵

Monomania

In 1831 Offord was charged with murder by shooting. He had the notion that inhabitants of the town of Hadleigh—especially the deceased—tended to deprive him of his liberty or life by continually issuing warrants against him. Found among his papers was an old summons at the foot of which he had written: "This is the beginning of an attempt against my life." In his pocket he carried a "list of Hadleigh conspirators against my life" with 40 to 50 names thereon, including that of the deceased. Several medical witnesses testified from the evidence they had heard at the trial that the defendant had monomania and that he committed the act while "under the influence of that disorder, and might not be aware that

in firing the gun, his act involved the crime of murder."

The jury was charged that to acquit on grounds of insanity it must find "that he did not know, when he committed the act, what the effect of it, if fatal, would be with reference to the crime of murder. The question was: did he know that he was committing an offense against the laws of God and nature." The jury acquitted him on grounds of insanity.

Non Compos Mentis

In 1840 Oxford was charged with treason. He had discharged a pistol at the carriage containing the Queen and Prince Albert. The carriage passed on, whereupon the defendant discharged another pistol toward it. Both shots missed. Another man was first seized and accused. At this point the defendant said, "It was me, I did it, I surrender myself."

The defendant had imagined himself to be a member of a non-existent, militant secret society and recorded imaginary meetings thereof. Several eminent medical men testified for the defendant, all to the effect that he was of unsound mind.

The jury acquitted him after being charged as follows: "Persons must be taken to be of sound mind until the contrary is shown. But a person may commit a criminal act and not be responsible. If some controlling disease was in truth the acting powers within him, which he could not resist, then he will not be responsible. It is not more important than difficult to lay down the rules. . . . On the part of the defense it is contended that the prisoner was *non compos mentis*, that is (as it has been said) unable to distinguish right from wrong, or, in other words, that from the effect of a diseased mind, he did not know at the time that the act he did was wrong. . . . Something has been said about the power to contract and to make a will. But I think that those things do not supply any test. The question is, whether the prisoner was laboring under that species of insanity which satisfies you that he was quite unaware of the nature, character and consequences of the act he was committing, or in other words, whether he was under the influence of a diseased mind, and was really un-

conscious,* at the time he was committing the act, that it was a crime."¹⁷

The U. S. Law of Criminal Responsibility

The extent to which the foregoing had been incorporated into law in the United States was evident in *U. S. v. Lawrence*. On January 31, 1835, Lawrence fired two percussion pistols at President Jackson.¹⁸ Only the caps of the pistols exploded, evidently owing to the ignorance of the assassin concerning the operation of the weapon.²⁰

A city magistrate made personal inquiry. He found a boarder in the house in which Lawrence roomed who had been convinced for some time that Lawrence was insane. Lawrence had attempted to kill his sister and brother-in-law, and there was evidence of grandiose delusions and paranoid ideation.¹⁹ On February 7, 1835, the marshal of the District of Columbia appointed two physicians to examine the defendant on the question of his sanity. (An editorial comment on the event in the local newspaper presumed Lawrence insane not by reason of the latter's personal history but from the nature of the act alone.²²) Their findings were reported in the local paper.²² However, they made no recommendation as to the defendant's sanity. This was solicited of them by the paper. Their reply cited "... such facts as we suppose would have superseded the necessity of expressing an opinion on the subject of his sanity ... laboring under extensive mental hallucination upon some subjects."

The trial was held on April 11, 1835. Francis Scott Key, prosecuting attorney, cited *Hadfield* and *Arnold* and left little doubt that a verdict of not guilty by reason of insanity would be welcome. The court handed the jury the verdict given in *Hadfield* that the defendant was "... not guilty having been under the influence of insanity at the time he com-

mitted the act." Following his acquittal²³ Lawrence was remanded "to be made as comfortable as possible until further accommodations could be made."

The McNaghten Case

On January 20, 1843, a Scotsman named McNaghten shot Drummond, the private secretary to Prime Minister Peel. Following Drummond's death resulting from the gunshot wound, a preliminary investigation was held on January 30. It appeared that McNaghten was convinced that the Tories were persecuting him; he was certain he had shot Peel.²⁴

At the trial on March 4 before three judges and a jury the Crown presented evidence of deliberate and intentional preparation for the commission of the crime.²⁵

At the conclusion of the Crown's case several physicians testified for the defense.

Dr. Munro testified:

"I do believe that the man was quite deprived of self-control. This deed was the crowning act of the delusion which had haunted him for years. That this may be a partial insanity only, is now clearly established. It may deprive a man of self-control. Monomania is quite distinct from general insanity. Nothing is more common than to find persons of great intelligence on many points quite insane on one point. I heard the evidence yesterday. It does not impair my opinion of his insanity in the least. I have known good arithmeticians among maniacs. I have often found them quite alive to the consequences of their deeds after the committal of them."

"Looking at the whole of this case I consider the prisoner quite capable of judging of the moral impropriety of his act."

Dr. McClure testified:

"My opinion is, that the act committed by him was the consequence of those delusions. From the whole history of the case I consider that his moral liability was destroyed."

Dr. Hutchinson testified:

"I have no doubt that he is laboring under morbid delusions of the mind. I consider that the delusions account for the act he has committed. He was perfectly incapable of exercising control in any matter connected with that delusion, and this act grew immediately out of the delusion."

Dr. Key testified:

"Persons may be laboring under a morbid delusion and yet may be perfectly capable of distinguishing right from wrong, but whatever act the delusion compels him to is quite beyond his moral control."

*Insanity caused by intoxication was not a defense to a criminal charge on the theory that such persons willfully deprive themselves of reason. Roscoe³ gives as an example of the foregoing soldiers "who have been severely wounded in the head who well know that excess makes them mad." "But if, by the long practice of intoxication an habitual or fixed insanity is caused, although this madness was contracted voluntarily, yet the party is in the same situation with regard to crimes, as if it had been contracted involuntary (sic) at first and is not punishable." The author here cites American cases and 1 Hale P.C. 32. Furthermore, although voluntary drunkenness cannot excuse the commission of a crime, where premeditation is at issue, intoxication of the defendant has been held to be a circumstance properly taken into consideration.¹⁸

Mr. Winslow, a surgeon, testified to the same effect.²⁵

Following the medical testimony the chief justice directed a verdict of acquittal.

Contemporary Commentary

Contemporary editorial commentary²⁵ criticized the court's intervention. It argued that in a civil commitment the Court would not prevent the lunacy commission from proceeding to hear further evidence and making its findings of fact. It attacked the physicians for confidently presuming to give an opinion on the state of mind of a person after an event at which they were not present.

Following the acquittal of McNaghten an outraged House of Lords propounded some questions of law to fifteen judges of the criminal courts of England. Their purpose was to clarify the law on criminal responsibility. The judges responded to these questions.²⁶ However, a judge and preeminent 19th century authority on the history of the criminal law of England, Stephen, wrote that the authority of the answers was questionable since it was not a judgment on evidence and the judges were under no obligation to answer the questions.

Partial Delusion

The first question had to do with "partial delusion." For example, a person thinks he is redressing a wrong or producing a public benefit: here the judges stated that he would be guilty "if he was acting contrary to the law of the land."

Question IV also concerned partial delusions. The answer given was that the defendant was to be judged "... as if the (delusion) ... were real." The example given was a person who thinks he is being attacked and defends himself accordingly. This answer assumes the delusion of McNaghten that he was being injured by Peel. Under this rule he would be guilty of first degree murder if he acted upon this delusion. The difficulty, as Stephen aptly points out, is that such delusions rarely stand alone.

Right or Wrong

Questions II and III concerned right or

wrong. Since all are presumed to know the law, this could not encompass solely the law of the land. The answer of the judges was that if the defendant is "... conscious that the act was one which he ought not to do and if that act was at the same time contrary to the law of the land, he is punishable" It would be for the jury to decide "... whether the accused had a sufficient degree of moral consciousness to know he was doing an act that was wrong"

Stephen points out that under this rule Hadfield would have been convicted. He concluded that the effect of delusions goes beyond the rules above promulgated. He notes that the rules are silent on whether the mind might be affected by delusions beyond resulting in mistaken basis for action. He implied that knowledge that an act was wrong might be interpreted in some other sense.²⁷

Stephen opined that madness should attenuate events as fever attenuates murder to manslaughter. He distinguished drunkenness from madness by the fact that drunkenness results from the defendant's own act. It was clear to him that criminal responsibility would not attach to acts occurring in a dream state.²⁸

Mental Disease

Summarizing consideration of criminal responsibility under the McNaghten rules, writing before the turn of the century, Stevens concluded²⁹ that "... the law of England ... is that a man who *by reason of mental disease is prevented from controlling his own conduct* is not responsible for what he does." (Emphasis added.) He concluded that if a narrower view of the rules is taken, madness is just "a possible cause of innocent mistakes."

Irresistible Impulse

Stephen defines self control in terms of the ability to attend distant goals. He also considered the question of irresistible impulse.³⁰ Here he suggested that defendants should be judged to have acted under irresistible impulses by "... whether disease has left them the power of comparing together the different motives by which their conduct may be af-

fects and so making a choice between them.”*

Indefinite Custody

Under the Criminal Lunatics Act of 1800 and the trial of Lunatics Act of 1883 defendants acquitted by reason of insanity in England (“guilty but insane”) were remanded to custody “at his majesty’s pleasure,” i.e., for an indefinitely long period with no right to release.³⁴ In 1964 this was amended to provide commitment as for the mentally ill in civil cases.³⁵

Summary

Prior to 1831 the reported cases on criminal responsibility in England appear to demonstrate that a jury would uniformly convict unless a verdict of acquittal was directed by the Court, as occurred in *Hadfield*.

Beginning with *Offord* and *Oxford*, juries seemed to accept the defense of insanity as more liberally defined by the Court.

*Stephen suggested³² that juries should have a choice of three verdicts in criminal cases: guilty, not guilty and “guilty, but his power of self control was diminished by insanity.”

In Scotland it has long been (and still remains) the law that juries may bring in verdicts of partial responsibility. The court thereupon sentences accordingly.³²

Not until 1957 did the criminal law of England undergo any such modification. In that year Parliament provided³³ for a third alternative verdict in homicide cases only. There the jury could find the defendant not guilty of murder but guilty of manslaughter instead “. . . if he was suffering from such abnormality of mind . . . as substantially impaired his mental responsibility for his acts . . .”

**New York Bar, the District of Columbia Bar and the Minnesota Bar.

Neither *Hadfield* nor *McNaghten* can be said to reflect popular sentiment, however, as both were directed verdicts. Indeed, the reaction of Parliament to the acquittal of *McNaghten* is a truer expression of the popular sentiment. Under the bidding of Parliament, rules were formulated which purported to restore the law of criminal responsibility to its former rigidity as surely as if the rules had been case law instead of extrajudicial pronouncements.

McNaghten brought to full flower the use of medical testimony as to a defendant’s sanity. *Laurence* in the United States reflected the same practice and provoked the same contemporary editorial condemnation. The *McNaghten* rules tend to restrict the scope of such inquiry into a defendant’s state of mind. Yet a foremost 19th century jurist, Stephen, while demonstrating the narrowness of the promulgated rules, unequivocally restated the ruling law of England in terms remarkably modern: one who by mental disease is prevented from controlling his own conduct is not responsible for what he does.

There is merit, therefore, in distinguishing between *McNaghten*, a case culminating in an early liberalizing trend in the law of criminal responsibility, and the *McNaghten* rules, a stultifying influence which persists.

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References

1. Russel, Wm. O.: Crimes and Indictable Misdemeanors, 2nd Ed., Philadelphia and Boston, 1831, Vol. 1 at 2.
2. Ibidem at 1, citing 1 Hale 14.
3. Roscoe, H.: A Digest of the Law of Evidence in Criminal Cases, 2nd Ed., Philadelphia, 1846 at 945.
4. Russel, supra, note 1 at 3.
5. Ibidem, 4-5.
6. 1 Rot. Par. 443 B.3 Edw 2 (1310), cited in Stephen, History of Criminal Law of England, Vol 2, Ch. XIX at 151, fn 1.
7. Medico-Legal Journal 32-33, 1964-5 at 176.
8. 16 How. St. Tr. 695 (1724).
9. 19 How. St. Tr. 886 (1760).
10. R. v. Hadfield, 27 St. Tr. 1321, reported in The Times, London, June 18, 1800.
11. Russel, supra, note 1 at 8.
12. The Times, London, May 16 et. seq., 1800.
13. Russel, supra, note 1, 9-10.
14. Ibidem at 9.
15. Roscoe, supra, note 3 at 946, citing 1 Collinson on Lunacy 636 and Shelford on Lunatics 462.
16. Rex v. Offord, 5 Car. & P. 168, 172 Eng. Rep. 924.
17. Regina v. Oxford, 9 Car. & P. 525, 173 Eng. Rep. 941.
18. Roscoe, supra, note 3 at 954.
19. Daily National Intelligencer, Washington, Jan. 31, et. seq., 1835.
20. Op. cit., February 2, 1835.
21. Op. cit., January 31, 1835.
22. Op. cit., February 9, 1835.
23. Op. cit., April 14, 1835.
24. The Times, London, January 21, et. seq., 1843.
25. The Examiner, London, March 11, 1843.
26. 10 C. & F. 200.
27. Stephen, supra, note Ch. XIX, passim.
28. Op. cit. 165-166.
29. Op. cit. at 167.
- 30-35 May be secured from the author or the reprints.

Money will buy a pretty good dog, but it won't buy the wag of his tail.

—Josh Billings

Business is business.

Says who? Says too many people.

You've probably heard it yourself many times.
It's used to justify almost *anything*.

But how many times have you ever questioned this attitude or raised your voice in protest? An idea like this takes root just because not enough people do anything to stop it.

If you have ever asked yourself "Why doesn't someone do something about it?" you're talking to the right person. You.

It won't be easy. Sometimes you'll need encouragement. The kind you'll find in your place of worship.

Here you'll discover you're not alone. That, in itself, can give you the strength to say "Says who?" once in a while when it needs to be said.



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Special Article

Cardiac Resuscitation in a Community Hospital

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St. Paul, Minnesota

A CARDIAC RESUSCITATION team can produce rewarding results in the community hospital. Cardiac arrest occurs in all areas of the hospital as well as in removed areas. Often attempts to restore a heart to normal function in the latter situation are futile because of lack of a well organized cardiac resuscitation team.

External cardiac massage was introduced by Jude, Kowenhoven and Knickerbocker in 1960.^{1,2} Prior to this time, cardiac asystole and ventricular fibrillation could occasionally be successfully treated by internal cardiac massage. This technique necessitated a thoracotomy. Applied in the operating room or postanesthesia room, open-heart massage could be rewarding; but if this emergency treatment was applied in an area other than the operating area, the results were rarely successful.

Since the introduction of external cardiac massage, the prognosis in cardiac arrest has been vastly improved.³ The present report is from a community hospital. The authors describe the cardiac resuscitation team organization, its plan of action and the results of the team effort. Bethesda Lutheran Hospital has 300 beds, an active intern program, but no residency program. In 1966 there were 12,000 admissions and 19,600 outpatients. The first patient to receive the benefits of this team effort had a cardiac arrest on April 18, 1964. This study begins on that date and extends through December 31, 1966, a period of 32 months.

Organization

Since the beginning of this effort, one of us (S.K.H.) has participated in many of the resuscitative attempts. In a typical community hospital, the staff members may not be immediately available during certain hours of the day. It has been necessary, therefore, to build the first line of defense around the nurse and

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the intern. At regular intervals during the year, lectures and demonstrations are given to the nursing and paramedical personnel, and each year the incoming interns are made familiar with the routine. It has been our experience that often the nurse and/or intern recognizes the emergency, sounds the alarm and starts external cardiac massage and oxygenation in less than a minute.

Procedure

As soon as a nurse discovers that a patient has suffered a cardiac arrest, she alerts the hospital switchboard operator to announce the key-call of "Code 99" over the public address system. At the same time, the personnel in attendance place a large chest board beneath the patient and initiate external cardiac massage and artificial respiration.

All members of the resuscitation team respond to the emergency call and often reach the patient in a maximum time of three minutes. Those persons responding to the call include all interns in the hospital at the time (a minimum of two), an anesthesiologist and/or nurse anesthetist, the electrocardiographic technician, the nursing supervisor, and the

head nurse of the nursing station involved. If there are any staff physicians in the hospital at the time, they also respond. Usually the first physician to arrive is an intern who takes command, continues the treatment started by the nurse, and delegates duties to incoming personnel.

Equipment

Chest Board and Ambu Resuscitator

Each of the nursing stations throughout the hospital is equipped with a chest board of 36" by 36" dimension, a tray containing oral airways and an Ambu resuscitator. This equipment is immediately available.

Anesthesia Machine

A portable, easily-moved Ohio-Heidbrink anesthesia machine and a resuscitation cart are kept in the intensive care unit and in the outpatient-emergency section. In response to the emergency call, the nursing personnel in the intensive care unit immediately transport these two items to the scene of emergency.

Resuscitation Cart

The resuscitation cart is equipped with the

TABLE I
Successfully Resuscitated, Discharged From Hospital

Case No.	Age	Sex	Diagnosis
1	68	F	Cerebral arteriosclerotic disease with convulsions
2	65	M	Coronary insufficiency
3	66	M	Postoperative nephrectomy (24 hours postoperatively)
4	70	F	Atrial fibrillation, cardiac decompensation
5	62	M	Carcinoma of the colon
6	60	F	Gastrointestinal bleeding, diabetes mellitus
7	60	M	Allergic reaction to dye for IVP
8	61	M	Asthma, respiratory failure
9	59	F	Congestive cardiac failure
10	59	F	Congestive cardiac failure
11	25	F	Barbiturate overdosage/suicide attempt
12	3	M	Convulsions, undetermined origin
13	62	M	Myocardial infarction
14	47	F	Coronary insufficiency, myocardial infarction
15	67	M	Gastrointestinal bleeding
16	67	F	ASHD, congestive cardiac failure, arrhythmia
17	73	F	Gastrointestinal bleeding
18	72	F	Cerebral thrombosis
19	59	M	Myocardial infarction
20	80	F	Myocardial infarction, cardiac decompensation

Advanced ages and severity of diagnosis of those patients who were successfully resuscitated and discharged from the hospital.

following items: a Morris defibrillator, a small Gomco suction machine, a laryngoscope with a full set of laryngoscopic blades, endotracheal tubes and airways, a sterile tray for doing a venous cut-down, intravenous Ringers lactate solutions, THAM, low molecular weight Dextran and 5 per cent dextrose/distilled water, the necessary syringes, needles and emergency cardiac drugs.

Results

Initial Response

During this study, there have been 119 resuscitation attempts. A total of 48 (40 per cent) cases responded initially to resuscitation. Twenty-eight patients expired during the following days as a result of their condition on admission.

Twenty patients completely recovered and were discharged (Table 1). None of these 20 showed any adverse effects from the arrest or from the resuscitation maneuvers. There was no nervous system impairment. Table 2 summarizes the results of this study, which are comparable to those of Lillehei and associates.³ Forty-five per cent of the patients who eventually left the hospital had originally been admitted with a diagnosis of cardiac disease.

Myocardial infarction was the cause of cardiac arrest in 20 per cent of the successful resuscitations.

Factor of Age

Review of the study reveals that age is no barrier to survival. The average age of the patients on whom resuscitation attempts were made was 61 years. The average age of the patients who were discharged was 66 years. All of the emergencies occurred on the various nursing stations in private and semi-private rooms. None of the reported cardiac arrests occurred in the operating room or recovery room.

The most dramatic result is that of Case 16. This 67-year-old woman was admitted to the hospital with a diagnosis of congestive cardiac failure. A total of 29 episodes of ventricular fibrillation were encountered in a 12-hour period, for which she received 43 defibrillation shocks. She was discharged from the hospital a month later, with no residual effects. The figure depicts an episode of cardiac arrhythmia in this patient that rapidly changed to ventricular fibrillation. Her heart was promptly defibrillated.



Figure—Case 16. Clinical electrocardiographic strip showing in *a*, pacemaker shift to the A-V node with coupled ventricular premature contractions, changing rapidly in *b* to ventricular tachycardia, and in *c*, to ventricular fibrillation.

TABLE 2
Summary of Results 1964-1966

Year	Total Number of Cases	Immediate Death		Response		Discharged	
		Number of Cases	Per Cent of Total	Number of Cases	Per Cent of Total	Number of Cases	Per Cent of Total
1964	35	18	51	17	49	8	23
1965	42	30	71	12	29	5	12
1966	42	23	54	19	46	7	17
Total	119	71	60	48	40	20	17

Results in first 32 months of cardiac resuscitation program. Twenty of the original 119 patients who arrested were discharged from the hospital with no residual effects.

Summary

Rewarding results in cardiac resuscitation can be accomplished through a well organized cardiac resuscitation team in a medium-sized community hospital.

Cardiac resuscitation was achieved in 40 per cent of 119 patients in a 32-month period. Of the 48 patients resuscitated, 20 (17 per cent) were discharged from the hospital. No pa-

tient who ultimately survived exhibited any significant nervous system impairment.

Thus in a 32-month period in this medium-sized community hospital, 20 patients with cardiac arrest were revived and left the hospital in good condition. It is likely that none or very few of these 20 patients would have survived without an organized cardiac resuscitation team.

References

1. Jude, J. R., Kowenhoven, W. B., and Knickerbocker, G. G.: Clinical and Experimental Application of New Treatment for Cardiac Arrest. *Surg Forum* 11:252, 1960.
2. Kowenhoven, W. B., Jude, J. R., and Knickerbocker, G. G.: Closed-Chest Cardiac Massage. *JAMA* 173:1064, 1966.
3. Lillehei, C. W., Lavadia, P. G., DeWall, R. A., and Sellers, R. D.: Four Years' Experience with External Cardiac Resuscitation. *JAMA* 193:651, 1965.

Errata

Porphyria, Strange and Baffling Ailment, by Drs. Shuman and Snively, concerning laboratory data, 50:10:1467, October, 1967.

The following corrections should be made. Porphobilinogen should be 3.2 mg./100 cc. and would be in the neighborhood of 50 mg. per day, assuming a 1500 cc. output. Delta aminolevulinic acid was 2.6 mg./100 cc., not per cc. On April 2nd, 1963, quantitative coproporphyrin was 3,311 mcg. per 24 hours. On June 14, 1963, porphobilinogen was negative to Watson Schwartz test.

Harry W. Shuman, M.D.

* * * *

Sweat Chloride Assay for Cystic Fibrosis—Leland Hansen et al., 50:8:1191, August, 1967.

The first sentence in the section on *Pre-Analysis Procedures* (page 1194) should read "Four ml. of diluent and 4 drops of gelatin reagent are added to the unknown sweat sample."

Warren J. Warwick, M.D.

Experience

Some doctors make the same mistakes for twenty years and call it clinical experience.—Noah Fabricant

We like a man that comes right out and says what he thinks when he agrees with us.—Anon

Minnesota State Board of Medical Examiners

Resolutions Adopted by Minnesota State Board of Medical Examiners on August 19, 1967

BE IT RESOLVED, that Minnesota State Board of Medical Examiners proposes that the Rules and Regulations of Minnesota State Board of Medical Examiners be amended in the following particulars:

1. ME 1 (f), by renumbering the same ME 1 (i).

2. ME 1 (g), by renumbering the same ME 1 (j).

3. ME 1, by adding thereto a new paragraph ME 1 (f), reading as follows:

“(f) ‘Medicine’ as used in MSA, § 147.10, shall mean and include any substance or agent which is:

- (1) intended for use or used in the diagnosis, treatment, prevention, mitigation or cure of any disease, bodily injury or infirmity; or
- (2) intended to affect or does affect the structure or function of any bodily organ or system,

whether the intended or actual effect of such substance or agent is at or remote from the site of administration. Except as otherwise expressly authorized by law, any person who for a fee prescribes, directs, or recommends for the use of any person any medicine, as herein defined, shall be deemed to be practicing medicine within the meaning of MSA, § 147.10.”

4. ME 1, by adding thereto a new paragraph ME 1 (g), reading as follows:

“(g) ‘Disease’ as used in MSA, § 147.10, shall mean and include any disorder, impairment, or infirmity in mental or physical ca-

capacity or in the physical, structural, or functional organization or character of any bodily organ or system.”

5. ME 1, by adding thereto a new paragraph ME 1 (h), reading as follows:

“(h) ‘Depressants’ and ‘Stimulants’ as used in MSA, § 147.02, subd. 3, shall include, but not be limited to, those drugs listed and described in MSA, § 152.01, subd. 5.”

6. ME 2, by striking and deleting the whole thereof and substituting the following in lieu and in place thereof:

“ME 2 *Application for Licensure for Medicine and Surgery*

(a) An application for admission to a licensing examination as provided in MSA, § 147.02 (which shall consist of both a written and oral examination, as provided in ME 3), shall be filed with the Board as hereinafter prescribed. If the Board finds that the application is complete and that all of the requirements of MSA, § 147.02, and of these regulations have been met, it shall advise the applicant of the date and place of the examination.

(b) Such application shall be submitted or forms prepared by the Board and shall include the following information:

- (1) If the applicant is a graduate of a medical or osteopathic college duly accredited by the Board, original or certified copy of diploma from such medical or osteopathic college, as the case may be, indicating that the applicant has satisfactorily completed a

- course of study acceptable to the Board and that he has received from such college the degree of Doctor of Medicine, Bachelor of Medicine, Bachelor of Medicine and Surgery or Doctor of Osteopathy.
- (2) If the applicant is currently enrolled in the fourth thirty-six (36) week session at a duly accredited medical or osteopathic college, a transcript of his credits, together with evidence, satisfactory to the Board, that the applicant has satisfactorily completed three entire sessions of a course of study acceptable to the Board of not less than thirty-six (36) weeks each at a duly accredited medical or osteopathic college. Prior to admission to the oral examination, the applicant shall file with the Board the original or a certified copy of diploma from a medical or osteopathic college duly accredited by the Board indicating that the applicant has satisfactorily completed a course of study acceptable to the Board and that he has received from such college the degree of Doctor of Medicine, Bachelor of Medicine, Bachelor of Medicine and Surgery or Doctor of Osteopathy.
 - (3) Original or certified copy of certificate of registration in the basic sciences issued by the Minnesota State Board of Examiners in the Basic Sciences.
 - (4) Evidence satisfactory to the Board of applicant's United States citizenship. In the event applicant is not a citizen, he shall submit, with his application, evidence that he has made a declaration of intent to become a citizen of the United States.
 - (5) A certificate of good moral character signed by two persons licensed to practice medicine and surgery by any recognized and accredited licensing authority within the United States or Canada.
 - (6) An unmounted recent photograph of the applicant with an affidavit on the reverse side thereof made by the applicant that the photograph is that of the applicant.
 - (7) Such other information as the Board shall, from time to time, deem necessary in order to evaluate the qualifications of the applicant.
- (c) An applicant who has passed the written examination in the clinical sciences of the National Board of Medical Examiners and who desires to take the oral examination, shall include in his application, in addition to the information required under ME 2 (b), evidence satisfactory to the Board that within one year before or five years after being granted the degree of Doctor of Medicine, Bachelor of Medicine, Bachelor of Medicine and Surgery or Doctor of Osteopathy, the applicant has satisfactorily passed the examination in the clinical sciences which is prepared, administered and graded in accordance with the provisions of MSA, § 147.02. The Board may, but shall not be required to, recognize and approve the results of such examination in the clinical sciences.
 - (d) An applicant whose credentials are determined by the Board to indicate ineligibility for examination shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by filing a statement of issues with the Board within twenty (20) days after receipt of such notice from the Board. After such hearing the Board shall notify the applicant in writing of its decision thereon.
 - (e) An applicant who has satisfactorily completed both the written and oral examinations, and who has fulfilled all the requirements of MSA, Chapter 147, and of these Rules and Regulations, shall be considered by the Board for licensure to practice medicine and surgery upon submitting to the Board evidence satisfactory to the Board that the applicant has satisfactorily completed either one year of graduate training in an institution in the United States or Canada approved for internship or graduate training by the Board or other graduate training approved by the Board.
 - (f) All applications for examination must be fully completed and forwarded to the Secretary of the Board postmarked not later than thirty (30) days before the date of the examination."

7. ME 3, by striking and deleting the whole thereof and substituting the following in lieu and in place thereof:

"ME 3 Conduct of Examinations Administered by the Board"

(a) Examinations administered by the Board shall be both written and oral. A written examination shall be given in surgery, medicine, obstetrics, gynecology, and such other branches as the Board may from time to time determine. Such written examination in the clinical sciences may be prepared, administered and graded by the Board or prepared and graded by the National Board of Medical Examiners and administered by the Board.

(b) Licensing examinations administered by the Board shall be conducted in accordance with the following rules, and any candidate violating such rules may be dismissed and barred from taking the examination, or may be otherwise disciplined.

(1) During the written examination no applicant shall communicate with any other person in any way except with the express permission of the person or persons conducting the examination.

(2) An applicant shall not bring books or help of any kind into the examination room.

(c) A grade of 75 shall be the passing grade on all examinations graded by the Board. A minimum general average of 75 in all subjects shall constitute a grade satisfactory for licensure. An applicant may fall below 75 in one subject and still be licensed by the Board. If an applicant falls below 75 in more than two subjects, it shall constitute a failure and require that the applicant retake the entire examination with passing grades in order to be eligible for licensure. An applicant failing two subjects may retake the two subjects at the next examination and upon receiving a minimum grade of 75 in each may be eligible for licensure.

(d) Upon the conclusion and grading of the examination, the Board shall prepare a report of the examination results and shall act on the report at its next meeting. The Secretary of the Board shall notify the ap-

plicant of the action of the Board on his application and examination."

8. ME 4 (b) (1), by adding thereto the following sentence:

"If the applicant is a graduate of a foreign medical school, the information required by ME 7 (a) (4) and ME 7 (a) (5)."

9. ME 4 (b) (2), by adding thereto the following sentence:

"If the applicant is a graduate of a foreign medical school, the information required by ME 7 (a) (2)."

10. ME 4 (b) (3), by striking and deleting the whole thereof and substituting the following in lieu and in place thereof:

"(3) Evidence satisfactory to the Board that the applicant has satisfactorily completed either one year of graduate training in an institution in the United States or Canada approved for internship or graduate training by the Board, or other graduate training approved by the Board."

11. ME 4, by adding thereto a new ME 4

(b) (4) reading as follows:

"(4) If the applicant is a graduate of a foreign medical school, evidence satisfactory to the Board that the applicant has been awarded a Certificate by The Educational Council for Foreign Medical Graduates, certifying to the applicant's formal education, his having passed the ECFMG English test and his having passed the ECFMG examination."

12. ME 4, by adding thereto a new ME 4

(b) (5) reading as follows:

"(5) The information required by ME 2 (e); ME 2 (b) (3); ME 2 (b) (4); ME 2 (b) (5); ME 2 (b) (6) and ME 2 (b) (7)."

13. ME 4 (c), by striking and deleting the whole thereof and substituting the following in lieu and in place thereof:

"(c) All applicants for licensure by reciprocity shall be required to pass an oral examination administered by the Board."

14. ME 4, by adding thereto a new ME 4

(d) reading as follows:

"(d) An applicant whose credentials are determined by the Board to indicate ineligibility for licensure shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by

filing a statement of issues with the Board within twenty (20) days after receipt of such notice from the Board. After such hearing the Board shall notify the applicant, in writing, of its decision thereon."

15. ME 5 (a), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(a) An application for a license to practice medicine and surgery by endorsement, without written examination, may be made by any applicant who is a diplomate of the National Board of Medical Examiners or of the National Board of Examiners for Osteopathic Physicians and Surgeons, or who has passed a licensing examination given by the appropriate board or agency of any state or country which the Board may from time to time determine to be acceptable, as provided in MSA §147.03; provided, however, that the Board may require the applicant to be examined in such subjects which, in the opinion of the Board, have not been satisfactorily covered."

16. ME 5 (b) (1), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(1) The information required by ME 2 (e); ME 2 (b) (3); ME 2 (b) (4); ME 2 (b) (5); ME 2 (b) (6) and ME 2 (b) (7)."

17. ME 5 (b), by adding thereto a new ME 5 (b) (3) reading as follows:

"(3) If the applicant is a graduate of a foreign medical school, evidence satisfactory to the Board that the applicant has been awarded a Certificate by The Educational Council for Foreign Medical Graduates, certifying to the applicant's formal education, his having passed the ECFMG English test and his having passed the ECFMG examination."

18. ME 5 (b), by adding thereto a new ME 5 (b) (4) reading as follows:

"(4) Evidence satisfactory to the Board that the applicant has satisfactorily completed either one year of graduate training in an institution in the United States or Canada approved for internship or graduate training by the Board, or other graduate training approved by the Board."

19. ME 5 (c), by striking and deleting the

whole thereof and by substituting the following in lieu and in place thereof:

"(c) All applicants for licensure by endorsement, except those who are diplomates of the National Board of Medical Examiners or of the National Board of Examiners for Osteopathic Physicians and Surgeons, shall be required to pass an oral examination administered by the Board."

20. ME 5, by adding thereto a new ME 5 (d) reading as follows:

"(d) An applicant whose credentials are determined by the Board to indicate ineligibility for licensure shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by filing a statement of issues with the Board within twenty (20) days after receipt of such notice from the Board. After such hearing the Board shall notify the applicant, in writing, of its decision thereon."

21. ME 6 (b) (6), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(6) If the applicant is a graduate of a foreign medical school, evidence satisfactory to the Board that the applicant has been awarded a Certificate by The Educational Council for Foreign Medical Graduates, certifying to the applicant's formal education, his having passed the ECFMG English test and his having passed the ECFMG examination."

22. ME 6 (e), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(e) An applicant whose credentials are determined by the Board to indicate ineligibility for such temporary permit or certificate shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by filing a statement of issues with the Board within twenty (20) days after receipt of such notice from the Board. After such hearing, the Board shall notify the applicant, in writing, of its decision thereon."

23. ME 7 (a) (1), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(1) The information required by ME 2 (b) (3); ME 2 (b) (6) and ME 2 (b) (7)."

24. ME 7 (a) (3), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(3) Evidence satisfactory to the Board of applicant's United States citizenship. In the event the applicant is not a citizen, he shall submit, with his application, evidence that he has made a declaration of intent to become a citizen of the United States."

25. ME 7 (a) (7), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(7) If the applicant submits to the Board evidence satisfactory to the Board that he has been awarded a Certificate by The Educational Council for Foreign Medical Graduates, certifying to the applicant's formal education, his having passed the ECFMG English test and his having passed the ECFMG examination, then applicant shall submit evidence satisfactory to the Board that the applicant has satisfactorily completed either one year of graduate training in an institution in the United States or Canada approved for internship or graduate training by the Board, or other graduate training approved by the Board. If the applicant has not been awarded such Certificate by The Educational Council for Foreign Medical Graduates, then applicant shall submit evidence satisfactory to the Board that the applicant has satisfactorily completed either two years of graduate training in an institution in the United States or Canada approved for internship or graduate training by the Board, or other graduate training approved by the Board."

26. ME 7 (b), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(b) As used herein, the term 'foreign medical school' shall mean a medical school located outside of the United States and Canada."

27. ME 7 (c), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(c) An applicant whose credentials are determined by the Board to indicate ineligibility

for examination shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by filing a statement of issues with the Board within twenty (20) days after receipt of such notice from the Board. After such hearing the Board shall notify the applicant, in writing, of its decision thereon."

28. ME 8 (b) (3), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(3) The information required by ME 2 (b) (3); ME 2 (b) (5); ME 2 (b) (6) and ME 2 (b) (7)."

29. ME 8 (c), by adding thereto the following sentence:

"The Board may, but shall not be required to, recognize and approve the results of an examination in the clinical sciences which is prepared, administered and graded by the National Board of Medical Examiners or may administer a recognized and approved examination prepared and graded by the National Board of Medical Examiners, in lieu of preparing, administering and grading the examination itself."

30. ME 8 (d), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(d) An applicant whose credentials are determined by the Board to indicate ineligibility for examination shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by filing a statement of issues with the Board within twenty (20) days after receipt of such notice from the Board. After such hearing the Board shall notify the applicant, in writing, of its decision thereon."

31. ME 9 (d), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(d) An applicant whose credentials are determined by the Board to indicate ineligibility for examination shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by filing a statement of issues with the Board within twenty (20) days after receipt of

such notice from the Board. After such hearing the Board shall notify the applicant, in writing, of its decision thereon."

32. ME 9 (g), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(g) An applicant whose credentials are determined by the Board to indicate ineligibility for registration shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by filing a statement of issues with the Board within twenty (20) days after receipt of such notice from the Board. After such hearing the Board shall notify the applicant, in writing, of its decision thereon."

33. ME 10, by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"ME 10 *Masseurs and Masseuses*

(a) An application for registration to practice massage as provided by MSA, § 148.36 shall be filed with the Board as hereinafter prescribed. If the Board finds that the application is complete and that all of the requirements of the statute and of these regulations have been met, it shall advise the applicant of the time, date and place of the interview.

(b) The application shall be made on forms provided by the Board and shall require the applicant to submit the following information:

- (1) Original or certified copy of birth certificate.
- (2) Evidence satisfactory to the Board of educational qualifications, including original or certified copies of degrees, diplomas or certificates, if any.
- (3) Evidence satisfactory to the Board of practical qualifications to practice massage.
- (4) Evidence satisfactory to the Board that the applicant is of good moral character.
- (5) An unmounted recent photograph with the affidavit of the applicant on the reverse side thereof that the photograph is that of the applicant.

(c) An applicant, prior to registration, shall

be interviewed by the Board in order to determine his eligibility for registration.

(d) An applicant whose credentials are determined by the Board to indicate ineligibility for registration shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by filing a statement of issues with the Board within twenty (20) days after receipt of such notice from the Board. After such hearing the Board shall notify the applicant, in writing, of its decision thereon.

(e) The Board, in its discretion, may register a person to practice massage in this state who holds a license from any other state or foreign country whose requirements for such license, as determined by the Board, are equivalent to those of the State of Minnesota. Such applicant shall submit, on forms provided by the Board, the following information:

- (1) The information required by ME 10 (b) (1) through (5).
- (2) Original or certified copy of license or certificate to practice massage issued by the state or country from which the applicant is seeking reciprocal licensure.

(f) Every person registered to practice massage in this state shall advise the Board in writing of the address of his place of residence and the address of each place at which he practices massage, and shall promptly notify the Board in writing of any change in either address."

34. ME 11 (e), by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"(e) An applicant whose credentials are determined by the Board to indicate ineligibility for examination shall be notified of such determination and the grounds therefor and may be granted a hearing thereon in accordance with the provisions of ME 63, by filing a statement of issues with the Board within twenty (20) days after receipt of such notice from the Board. After such hearing the Board shall notify the applicant, in writing, of its decision thereon."

35. ME 62, by striking and deleting the whole thereof and by substituting the follow-

ing in lieu and in place thereof:

"ME 62 *Accusation* A hearing to determine whether a right, license or privilege should be revoked, suspended, limited or conditioned, shall be initiated by the issuance of an accusation by the Board. The accusation shall be a written statement of charges which shall set forth in ordinary and concise language the acts or omissions with which the respondent is charged and shall be in sufficient detail to enable the respondent to prepare his defense. It shall specify the statutes and rules which the respondent is alleged to have violated. The accusation may also include any additional information which the Board deems appropriate. The accusation shall be verified by a member of the Board. The verification may be on information and belief."

36. ME 63, by striking and deleting therefrom the last four sentences thereof, and by substituting the following in lieu and in place thereof:

"If the Board is the initiating party, the statement of issues shall be served in the same manner as an accusation, and shall be accompanied by a Notice of Hearing substantially in the form set forth in ME 66. If the applicant is the initiating party, the statement of issues shall be served on the Board by registered or certified mail, addressed to the Board at its office in St. Paul, Minnesota, and such service shall be deemed a request for hearing. Within ten (10) days after such service, the Board shall deliver or mail to the applicant a Notice of Hearing, substantially in the form set forth in ME 66. In either case, the hearing shall be held not less than twenty (20) days nor more than one hundred twenty (120) days after service of the statement of issues. Hearings shall be held in St. Paul, Minnesota, at a place designated by the Board, unless the parties, by agreement, select another place within the State of Minnesota."

37. ME 64, by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"ME 64 *Service of Accusation; Form, Manner and Proof*

(a) Upon the issuance of an accusation, the Board shall serve a copy thereof on the re-

spondent as provided in ME 64 (b) hereof.

(b) If the respondent is a resident of the State of Minnesota and can be found therein, the accusation and all accompanying information shall be served upon respondent personally in the manner provided by law for the service of a summons in a civil action. If the respondent is not a resident of the State of Minnesota, or if the respondent is a resident of the State of Minnesota but cannot be found therein, the accusation and all accompanying information shall be served upon respondent by registered or certified mail, addressed to the most recent address theretofore furnished by the respondent to the Board, and the same shall be deemed received by respondent five (5) days after having been deposited in the United States mail, postage prepaid, addressed to such address. The appearance of respondent in the proceeding shall constitute a waiver of any defect in such service. Service may be proved by the affidavit of the person making the same."

38. ME 65, by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"ME 65 *Time and Place of Hearing* The Board shall determine the time and place of the hearing on the accusation which shall be held not less than twenty (20) days nor more than one hundred twenty (120) days after service of the accusation upon the respondent. The hearing shall be held in Saint Paul, Minnesota, at a place designated by the Board, unless the parties, by agreement, select another place within the State of Minnesota."

39. ME 66, by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"ME 66 *Notice of Hearing* A Notice of Hearing on the accusation shall be served by the Board upon respondent at the same time and in the same manner as the service of the accusation. The Notice of Hearing shall be substantially in the following form:

You are hereby notified that a hearing will be held before Minnesota State Board of Medical Examiners at
..... on
19...., at the hour of M.,

o'clock, upon the charges made in the accusation served upon you. You may be present at the hearing; may be, but need not be, represented by counsel of your own choosing; may present any relevant evidence on your own behalf and will be given full opportunity to cross-examine all witnesses who testify therein. If you fail to appear at the time and place above set forth, such failure will constitute a waiver of your right to a hearing, and Minnesota State Board of Medical Examiners may proceed upon the accusation with or without a hearing."

40. ME 71, by striking and deleting the whole thereof and by substituting the following in lieu and in place thereof:

"ME 71 *Form of Decision; Findings* Every decision and order adverse to a party to the proceeding shall be in writing and, except when such decision or order is made pursuant to stipulation with or the consent of the respondent, shall contain a statement of findings or reasons, a determination of the

issues presented, and the penalty, if any, or decision of the Board. The findings shall consist of a statement of the conclusions upon each contested issue of fact necessary to the decision. Parties to the proceedings shall be notified of the decision and order in person or by mail. A copy of the decision and order and accompanying statement of reasons together with proof of service shall be delivered or mailed, upon request, to the respondent or to his attorney of record."

BE IT FURTHER RESOLVED, that a public hearing on the adoption of the foregoing proposed changes in the Rules and Regulations of the Minnesota State Board of Medical Examiners be held on Saturday, February 17, 1968, at ten o'clock a.m. in Room 496, Lowry Medical Arts Building, St. Paul, Minnesota.

BE IT FURTHER RESOLVED, that notice of such hearing be given by the Secretary of this Board pursuant to the provisions of Minnesota Statutes, 1965, § 15.0412.

Thirty-First Annual Meeting The New Orleans Graduate Medical Assembly

The thirty-first annual meeting of The New Orleans Graduate Medical Assembly will be held March 4, 5, 6, 7, 1968, headquarters at The Roosevelt Hotel.

Nineteen outstanding guest speakers will participate and their presentations will be of interest to both specialists and general practitioners. The program will include fifty-one informative discussions on many topics of current medical interest, in addition to a clinicopathologic conference, symposia, medical motion pictures, round-table luncheons, and technical exhibits. This program is acceptable for thirty-two (32) elective hours by the American Academy of General Practice.

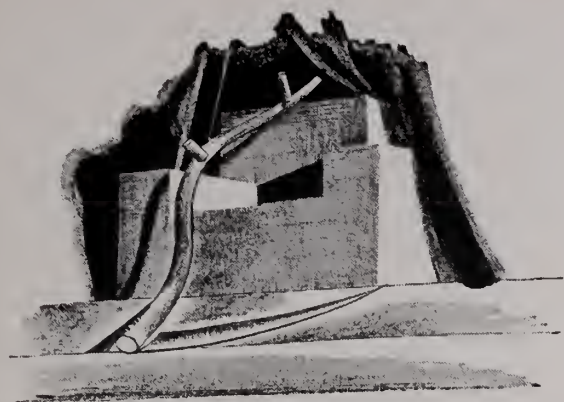
An interesting and enjoyable program of entertainment for visiting ladies has been planned.

Of special interest will be a one-day pre-Assembly symposium scheduled for Sunday, March 3 on "Sexual Problems in Clinical Practice." Six papers, together with a panel discussion, will be presented by six authorities on this subject.

Illness

Illness does not come from without; man creates it for himself, uses the outer world merely as the instrument with which to make himself ill, selects from that inexhaustible supply to be found in the wide world, now the spirochete of syphilis, today a piece of orange peel, tomorrow the bullet of a revolver, the day after a chill, so that he may pile on his woes. And always for the sake of getting pleasure out of it, because as a human being he finds a natural pleasure in suffering; because as a human being he has by nature a feeling of guilt, and wants to remove it by self-punishment; because he wants to escape from something or other that is uncomfortable.

—Georg Groddeck



RUSSELL H. FROST, M.D.

Dr. Russell H. Frost, 67, Edina physician and a former superintendent and medical director of Glen Lake Sanatorium, died Friday, October 27, following a prolonged illness.

The tuberculosis and pulmonary disease specialist was graduated from the University of Minnesota Medical School in 1924. He served his internship at Ancker Hospital, St. Paul.

He was a former superintendent and medical director of Buena Vista Sanatorium, Wabasha, Minnesota, the G. B. Cooley Sanatorium, Monroe, Louisiana. During World War II, Dr. Frost served in the U. S. Navy Medical Corps in the South Pacific and held the rank of Commander at the time of his discharge.

Dr. Frost was a member of the Hennepin County Medical Society, Minnesota State and American Medical associations, Minnesota and American Trudeau Medical Societies and the American College of Chest Physicians. He is a past secretary and president of the Wabasha County Medical Society, president of the Minnesota Trudeau Medical Society, and president of the Minnesota Chapter of the American College of Chest Physicians.

He was a former member of the Minnesota State Medical Association's Committee on Tuberculosis and a member of the Tuberculosis and Health Association of Hennepin County Board of Directors.

He is survived by a son and three daughters.

ERNEST M. HAMMES, M.D.

Dr. Ernest M. Hammes, 83, St. Paul neurologist and psychiatrist and former faculty member at the University of Minnesota medical school died September 30, in his home. Born in New Trier, Minnesota, he graduated from the University of Minnesota Medical School. Graduate work in neurology and psychiatry was done in Frankfurt, Germany, and Vienna, Austria.

Dr. Hammes was a past president of the Ramsey County Medical Society and a Life Member, 50-Club member and past president of the Minnesota State Medical Association. He was the recipient of the Distinguished Service Award in 1958. Also, Dr. Hammes was a member of the American Neurologic Association, a past president of the Central Neuropsychiatric Association and a charter member of the American Board of Neurology and Psychiatry. He was a former president of the Blue Shield of Minnesota and was a member of its board of directors from 1947 until his retirement.

He is survived by his wife, two daughters and a son, Dr. Ernest M. Hammes, Jr., of St. Paul.

In Memoriam

*There's nothing terrible in death;
'Tis but to cast our robes away,
And sleep at night, without a breath
To break repose 'till dawn of day.*

Montgomery

WILLIAM EMORY PROFFITT, M.D.

Dr. William E. Proffitt, 52, Minnesota Twins baseball team physician for the past seven years, died unexpectedly in his sleep, September 30. Born in Danville, Illinois, Dr. Proffitt received his medical degree from the University of Minnesota.

Dr. Proffitt had practiced medicine in Minneapolis for more than thirty years. Former Governor Orville Freeman had appointed him Chairman of the Governor's Council on Youth Physical Fitness and he was reappointed by former Governors Elmer L. Andersen and Karl F. Rolvaag, and Governor Harold LeVander.

He was a member of the Hennepin County Medical Society, American Medical Association and the Minnesota State Medical Association.

He is survived by his wife, a son and a daughter.

THEODORE H. SWEETSER, M.D.

Dr. Theodore H. Sweetser, Sr., 74, former head of the urology departments at St. Mary's and Hennepin County General hospitals, died October 8. A graduate of Central High School, the University of Minnesota and the Columbia University College of Physicians and Surgeons, Dr. Sweetser was a pioneer in correcting bladder defects in infants.

He was a past president of the Minnesota Academy of Medicine and a vice president of the State Board of Health and Vital Statistics. He taught pathology and surgery at the University of Minnesota from 1919 until his retirement in 1962.

Mayor Arthur Naftalin presented Dr. Sweetser with the distinguished service award in 1962 for his years of teaching and medical service to Minneapolis.

He was a member of the Hennepin County Medical Society, and American Medical Association, and a Life Member of the Minnesota State Medical Association.

He is survived by his wife, three daughters and two sons, one of whom is Dr. Theodore H. Sweetser, Jr., of Minneapolis.

DONALD C. VROMAN, M.D.

Dr. Donald C. Vroman, 53, anesthesiologist, died August 3 in Omaha, Nebraska. He was born in Omaha and received his medical degree from the University of Nebraska College of Medicine.

He was a member of the Hennepin County Medical Society, American Medical Association and the Minnesota State Medical Association. He also taught at the University of Nebraska College of Medicine.

He is survived by his wife and three sons.



Indications: Hypertension and many types of edema involving retention of salt and water.

Contraindications: Hypersensitivity and most cases of severe renal or hepatic disease.

Warning: With the administration of enteric-coated potassium supplements, which should be used only when adequate dietary supplementation is not practical, the possibility of small bowel lesions (obstruction, hemorrhage, and perforation) should be kept in mind. Surgery

for these lesions has frequently been required and deaths have occurred. Discontinue enteric-coated potassium supplements immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occur.

Use with caution in pregnant patients, since the drug may cross the placental barrier and adverse reactions which may occur in the adult (thrombocytopenia, hyperbilirubinemia, altered carbohydrate metabolism, etc.) are potential

problems in the newborn.

Precautions: Antihypertensive therapy with Hygroton should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents or other potent antihypertensive drugs, or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. Barbiturates, narcotics or alcohol may potentiate hypotension. Because of the possibility of progression of renal damage, peri-

odic determination of the BUN is indicated. Discontinue if the BUN rises or liver dysfunction is aggravated. Hepatic coma may be precipitated.

Electrolyte imbalance, sodium and/or potassium depletion may occur. If potassium depletion should occur during therapy, Hygroton should be discontinued and potassium supplements given, provided the patient does not have marked oliguria.

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severe ischemic heart disease and in patients receiving corticosteroids, ACTH, or digitalis. Salt restriction is not recommended.

Adverse Reactions: Nausea, gastric irritation, vomiting, anorexia, constipation and cramping, dizziness, weakness, restlessness, hyperglycemia, hyperuricemia, headache, muscle cramps, orthostatic hypotension, aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, impotence, dysuria, transient myopia, skin rashes, urti-

caria, purpura, necrotizing angitis, acute gout, and pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration. Other reactions reported with this class of compounds include: jaundice, xanthopsia, paresthesia, and photosensitization.

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THREE MAN group in North West Wisconsin Resort, State Conservation and Retirement Area needs two more physicians adequately to serve their practice. Facilities offered are three-room physician suites, X-ray and lab under AMT technician, RN-only nursing personnel. New accredited thirty-two bed hospital and forty-six bed nursing home. Deer and duck hunting, fishing within five minutes of town. Internist most needed; generalists welcomed. Will meet any reasonable salary request. Partnership after one year. Write: MINNESOTA MEDICINE—365; 375 Jackson St., St. Paul 55101.

WANTED: GP to join clinic serving population area of 12,000. City has new hospital, new clinic building, two nursing homes, new Jr-Sr high school, new swimming pool, rich farming area in Red River Valley. Fishing and hunting nearby; metropolitan city close by. Salary open and partnership if interested. Write or call Warren Clinic, Warren, Minnesota 742-6231, area code 218.

WANTED: General practitioner, to join two G.P.'s well established in north central Minnesota community, 2200 pop., 65 miles from Twin Cities. Excellent office space with lab and X-ray, just opened new hospital, all facilities. Assistantship or partnership. Considerable surgery and obstetrics. Hunting, fishing, golf club. Great opening for interested G.P. WRITE MINNESOTA MEDICINE—381; 375 Jackson, St. Paul, 55101.

GENERAL PRACTITIONER wanted to join well-established practitioner. New clinic building—90 miles east of St. Paul—city of 14,000. Early partnership with full hospital facilities. Ideal location. L. W. Picotte, M.D.; Chippewa Falls, Wisconsin.

INTERNIST AND GENERAL PRACTITIONER wanted to join a five-man clinic group in Minneapolis. Complete laboratory and X-ray with board roentgenologist. Excellent hospital staff associations. Salary arrangement to start with early partnership. Write: MINNESOTA MEDICINE—289; 375 Jackson, St. Paul, 55101.

Classified Advertisements

GENERAL PRACTITIONER OR INTERNIST needed in six man group in Northeastern Minnesota. 38 bed accredited hospital next door to modern clinic, rotating call schedule, over 4 wks. vacation per year, study and sick leave, group paid disability and retirement plans, and full partnership in 6 months. Starting guarantee \$18,000 to \$22,000 with increases to \$26,000 to \$28,000 over 4 years. Ideal opportunity for man desiring association with active group in small community offering good income plus ample time off. Contact Harold B. Leppink, M.D., Community Clinic, Two Harbors, Minnesota. Phone Area 218 834-2171.

MORGAN, MINNESOTA, Wants a General Practitioner. Opportunity to take over a well established practice. Physician recently retired after practicing here for 33 years. Progressive community in the best rural area of Southern Minnesota. New medical clinic building just completed. Call or write M. L. Kuhn, Morgan, Minnesota. Tel. Morgan #73 or #99.

WANTED: INTERNIST to enlarge busy internal medicine department in highly successful nine man specialty group. All are board certified. Well equipped lab and x-ray—new 120-bed hospital. Pleasant community of 15,000 plus on Mississippi River. Good recreational facilities, not far from Twin Cities. Salary one year then partnership. Write: George E. Jackish, M.D.—Interstate Clinic, Red Wing, Minnesota or call 507 388-3503.

WANTED: Locum Tenens for general practice for February, 1968. Salary open. Contact: Maurice Meller, M.D., Brainerd Clinic, Brainerd, Minnesota.

PHYSICIAN INTERESTED in internal medicine wanted for Medical Service. Starting salary \$12,873 to \$17,221, depending on qualifications. Liberal fringe benefits. Non-discrimination in employment. Contact Chief of Staff, Veterans Administration Hospital, Des Moines, Iowa 50308.

WANTED: Young, energetic General Practitioner to join one man clinic. Salary open. Contact: Maurice Meller, M.D., Brainerd Clinic, Brainerd, Minnesota.

WANTED: YOUNG PHYSICIAN for association leading to partnership with four well-established General Practitioners in fast-growing suburb of St. Paul. Excellent clinic facilities in nearly new, partnership owned, well equipped, medical center building. Contact: A. Eugene Muller, M.D., North St. Paul Medical Center, 2579 East 7th Avenue, North St. Paul, Minnesota 55109.

WANTED: G.P. to take over practice located in East Side of St. Paul, including equipment and lease, all available with good financing. Retiring G.P. will practice to acquaint buyer with patients. Write: MINNESOTA MEDICINE—386, 375 Jackson, St. Paul 55101.

(Continued)

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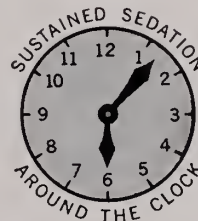
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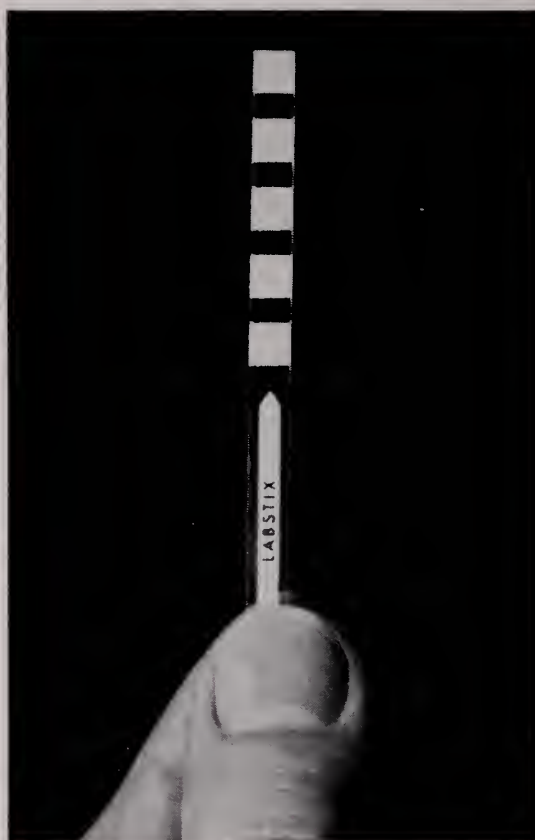
PHYSICIAN WANTED: G.P. with additional surgical and OB experience—desired to associate with two G.P.'s with similar experience in large, well established practice in Central Minnesota. Hospital accredited, 300 bed, open staff, complete services. Salary leading to partnership. Adequate housing in area. Send background information, professional and personal to: MINNESOTA MEDICINE-283, 375 Jackson, St. Paul 55101.

INTERNIST ASSOCIATE wanted in Pacific Northwest city of 170,000. Low humidity, no ragweed, fabulous recreational area. Expanding practice to accommodate second internist. New multi-specialty building adjacent new hospital in residential area. All hospitals open staff. Further details by correspondence only. Give curriculum vitae first letter. Write: MINNESOTA MEDICINE-382, 375 Jackson, St. Paul 55101.

MEDICAL GAL FRIDAY: R.N. desires position in Drs. office in St. Paul loop area 5 days a week. No Sat. Former surg. nurse; 5 yrs. experience in Drs. clinics; 11 mos. experience processing Military Medicare claims, lite typing, no shorthand or dictaphone exper. Good references. Salary needed \$450-\$500. Phone 755-3951 after 6 P.M.

PSYCHIATRIC RESIDENCIES: Accepting applications for January and July 1968. Balance didactic-clinical program providing extensive, varied experience with both inpatient and outpatient adults and children. Fully approved three year training. Three year plan: \$8,978, \$9,417, \$10,210. Five year career plan: \$10,231, \$11,797, \$13,739, \$17,497, \$18,458. Located in Michigan's serene, scenic water wonderland. Contact: Dr. Paul E. Kauffman, Director of Training, Traverse City State Hospital, Traverse City, Michigan 49684. An equal opportunity employer.

GENERALIST AS MEMBER of Medical Staff of progressive State Hospital in Michigan's Vacationland. Hospital has 3-year accreditation, JCAH and 3-year residency accreditation by A.P.A. Salary \$16,000 to \$19,800. Excellent fringe benefits. Civil Service Security when qualified. Apply L. B. Young, M.D. Director of Medical Services, Traverse City State Hospital, Traverse City, Michigan 49684.



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(Continued)

PHYSICIAN NEEDED to serve as Chief Medical Director for State Prison at Stillwater. 50-bed hospital, laboratory technician, registered nurses. Salary ranges from \$13,344 to \$18,972 per year. Full time, permanent position under Minnesota State Civil Service. Contact: L. D. Jones, Minnesota State Prison, Box 55, Stillwater or call 439-1910, Ext. 320.

INTERNIST WANTED: Central Wisconsin city of 35,000 needs internist badly. Solo practice, association with small group or large clinic available. Contact G. H. Brister, M.D., Medical Arts Bldg., Wausau, Wisc.

SENIOR PARTNER retiring and wish another physician to join busy general practice. L. T. Winninger, M.D., 601 Baltimore St., Waterloo, Iowa 50702.

WANTED: Ophthalmologist to fill vacancy with well established eight man group. Beautiful award winning clinic just blocks from new 120 bed hospital. Picturesque community of 15,000 located on the Mississippi River with good recreational facilities, schools and churches. An excellent opportunity in a growing environment. Salary one year, then partnership. Write Harry Williams, M.D., Medical Block Clinic, Red Wing, Minnesota, or call 507, 388-4751.

RESIDENT desires locum tenens January and February or January and March. Twin Cities area. Call 721-7512, Extension 307. John H. Mahler, M.D., 5761 33rd Avenue South, Minneapolis.

GENERAL PRACTITIONER with 25 years experience and a well-established practice in a suburb of the city desires a General Practitioner with an association towards a partnership. Write: MINNESOTA MEDICINE-389, 375 Jackson, St. Paul 55101

WANTED: Board-eligible or board-certified obstetrician-gynecologist with military obligation completed, to associate with a group of three board-certified obstetrician-gynecologists in Twin City area. Write: MINNESOTA MEDICINE-390, 375 Jackson, St. Paul 55101.

The Nobel Conferences

Fourth annual Nobel Conference is to be held January 10-11, Gustavus Adolphus College in St. Peter. The 1968 theme is "The Uniqueness of Man."

Contact: James Wennblom at the College for information.



Mark Waters was a chain smoker. Wonder who'll get his office?

Too bad about Mark. Kept hearing the same thing everyone does about lung cancer. But, like so many people, he kept right on smoking cigarettes. Must have

thought, "been smoking all my life... what good'll it do to stop now?" Fact is, once you've stopped smoking, no matter how long you've smoked, the body begins to reverse the damage done by cigarettes, provided

cancer or emphysema have not developed. Next time you reach for a cigarette, think of Mark. Then think of your office —and your home.

American Cancer Society 

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Ad No. 0267-D (3 cols. x 115 lines)



Meetings and Announcements

A work of real merit finds favor at last.—A. B. Alcott

DECEMBER

- Minnesota OB-GYN Society, St. Paul-Ramsey Hospital, 9:00 A.M., December 2.
- Southwestern Minnesota Medical Society, December 4, Ehlers Supper Club, 7:00 P.M.
- Scott-Carver County Medical Society, December 5, Wagner Supper Club, Jordon, Minnesota, 7:30 P.M.
- St. Louis County Medical Society Executive Committee, St. Luke's Hospital, 6:00 P.M., December 14.
- Annual Banquet, Kitchi Gammi Club, 7:30 P.M., December 16.
- McLeod County Medical Society, December 21.
- Minnesota Academy of Ophthalmology and Otolaryngology. No date set as yet.
- American Academy for Cerebral Palsy, San Francisco-Hilton Hotel, San Francisco, Dec 10-14. Exec. Sec.: J. D. Russ, M.D., 1520 Louisiana Ave., New Orleans 70115.
- American Academy of Dermatology, (E), Palmer House, Chicago, Dec. 2-7. Sec.-Treas.: Stanley E. Huff, M.D., 636 Church St., Evanston, Ill. 60201.
- American Association for the Advancement of Science, New York, Dec. 26-31. Info: Dr. L. Taylor, 1515 Massachusetts Ave., N.W., Washington, D. C. 20005.
- American Psychoanalytic Association, (E) (M) Waldorf Astoria Hotel, New York, Dec. 15-17. Exec. Sec.: Mrs. Helen Fischer, One E 57th St., New York 10022.
- Delaware Academy of General Practice, (E), Delaware Academy of Medicine, Wilmington, Dec. 2. Sec.: Charles W. Wagner, 1925 Lovering Ave., Wilmington, Del. 19806.
- Latin American Congress of Pathology (VI) and Pan American Meeting of International Academy of Pathology (I), (E), San Jeronimo Hilton, San Juan, PR, Dec. 10-17. Info: Raul A. Marcial-Rojas, M.D., Pres., School of Medicine, San Juan, PR 00905.
- New York State Society of Anesthesiologists, New York Hilton Hotel, New York, Dec. 11-13. Exec. Sec.: Mrs. Eugenia C. Sinisi, 30 E. 42nd St., New York 10017.
- Society of Cosmetic Chemists, Semi-annual, Americana Hotel, New York, Dec. 6. Info: Mrs. Eunice T. Miner, Adminis. Asst., 2 E. 63rd St., New York 10021.
- Southern Surgical Association, The Homestead, Hot Springs, Va., Dec. 4-6. Exec. Sec.: Dr. George H. Yeager, 314 Medical Arts Building, Baltimore 21201.

JANUARY

- American Academy of Orthopaedic Surgeons, [E], Palmer House, Chicago, January 20-25. Exec. Sec.: John K. Hart, 29 E. Madison, Chicago 60602.
- American Group Psychotherapy Association, [E] La Salle Hotel, Chicago, January 24-27. Adm.-Sec.: Mrs. Marilyn Schiff, 1790 Broadway, New York 10019.
- American Rheumatism Association, (Interim Meeting) Baltimore, Md., January 17-18. Info.: Miss Margaret M. Walsh, 1212 Avenue of the Americas, New York 10036.
- American Society for Surgery of the Hand, Palmer House, Chicago, January 19-20. Sec.-Treas.: Raymond M. Curtis, M.D., 2947 St. Paul St., Baltimore 21218.
- Health Physics Society, Midyear Topical Symposium (Sponsored by the Savannah River Chapter) "Environmental Surveillance in the Vicinity of Nuclear Facilities," Augusta Town House, Augusta, Ga., January 24-25. Info: Arrangements, J. H. Horton, Radiological and Environmental Sciences Div., Savannah River Lab., Aiken, S. C. 29801.
- Los Angeles Radiological Society (20th Annual Mid-winter Conference) International Hotel, Los Angeles, January 27-28. Info.: Duane I. Gillum, M.D., Good Samaritan Hospital, 1212 Shatto St., Los Angeles 90017.
- Research Study Club of Los Angeles Annual Mid-winter Convention, in Ophthalmology and Otolaryngology, Statler Hilton Hotel, Los Angeles, January 21-26. Sec.: Burns C. Steele, M.D., 1411 W. Olive Ave., Burbank, Calif. 91506.
- Society of Thoracic Surgeons, [E], Roosevelt Hotel, New Orleans, January 29-31. Exec. Sec.: Frances X. Byron, M.D., City of Hope Medical Center, 1500 E. Duarte Rd., Duarte, Calif. 91010.

FEBRUARY

- American Academy of Allergy, [E], Statler-Hilton, Boston, February 3-7, Exec.-Sec.: Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 53202.
- American Academy of Occupational Medicine, Marriott Twin Bridges Motel, Washington, D. C., February 7-9. Exec. Sec.: Bertram D. Dinman, M.D., Institute of Industrial Health, University of Michigan Medical Center, Ann Arbor, Mich. 48104.



The Arthritis Foundation salutes the thousands of dedicated physicians who volunteer their services in the nation's fight against crippling arthritis.

The Arthritis Foundation is the sole national voluntary health agency committed to conquering the rheumatic diseases. It provides the means for dynamic partnership between physicians and laymen to marshal leadership and resources toward the solution of this major national health problem.

The Arthritis Foundation looks forward to rapid growth with increasing opportunity for physicians to participate in the arthritis movement. For further information about The Arthritis Foundation and its programs write to the Foundation chapter in your community or to the Medical Department, Box 2525, New York, N.Y. 10001.

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Rheumatism Association Section

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Medical Director



Physician's Diary

Two faculty members of the University of Minnesota Medical School, **Doctors James F. Koerner and James H. Moller**, were named 1967 winners of the Minnesota Medical Foundation Distinguished Faculty Teaching Awards.

* * *

Dr. and Mrs. J. E. Schroepel were given a plaque as the annual Citizen's Award for thirty years of service to Winthrop.

* * *

A St. Paul, Minnesota Physician, **A. Frank Adair, M.D.**, will return in mid-October from work in Project HOPE's medical teaching-treatment mission to Cartagena, Colombia. He worked as a volunteer aboard the floating medical center S. S. HOPE.

* * *

Dr. Edward H. Soule, a member of the Section of Surgical Pathology of the Mayo Clinic, was awarded the gold medal, given for the best educational exhibit, of the American Society of Clinical Pathologists at the annual meeting of that society in Chicago in December. The title of the exhibit was "Primary Tumors of the Soft Tissues of the Extremities."

* * *

The following physicians were inducted as new Fellows of the American College of Surgeons in October: **Doctor Lynn C. Stoker** of Albert Lea; **Doctors Eugene F. Bernstein, Aldo R. Castaneda, Harrison H. Farley, John H. Glaeser, Hermann W. Heupel, Richard E. Larson, Arnold S. Leonard, Richard R. Lund, Donald G. McQuarrie, Demetre M. Nicoloff, Hyman M. Paisner, David E. Raab and Melvin E. Sigel** of Minneapolis; **Doctor John N. Simons** of Rochester; **Doctors Bernard Gooft, Max E. Harris and George T. Tani** of St. Paul and **Frederick C. Wuest** of Wayzata.

* * *

New Locations: **Dr. Cyril J. Dillenburg** has joined the staff of St. Francis and Bethesda Hospitals in Crookston. . . . **Dr. E. P. Bryant** has left the Ellendale Clinic to enter into a group practice in Silver Bay. . . . **Dr. Roger J. Benjamin** has opened up a private medical practice in Owatonna. . . . **Doctors**

Gregory and Wanda Kaminski have joined **Dr. S. F. Ceplecha** in Redwood Falls.

* * *

Dr. Frederick Van Bergen, head of the University of Minnesota's Department of Anesthesiology, was named president of the Academy of Anesthesiology at the Academy's 36th annual meeting in Scottsdale, Arizona, in September.

* * *

Walter F. Larrabee, Jr., M.D., is the acting medical director at the Willmar State Hospital. He succeeded **Dr. Donald C. Carter** who resigned to assume a full-time faculty position at the University of Missouri school of medicine.

* * *

Dr. L. K. Onsgard was honored by the residents of Houston upon occasion of his leaving Houston after thirty-seven years of service. Dr. and Mrs. Onsgard will reside in St. Petersburg, Florida.

* * *

Dr. Malcolm Dockerty, a Mayo Clinic pathologist, has received an honorary doctor of laws degree from his alma mater, Prince of Wales College, Prince Edward Island, Canada.

* * *

A Grand Marais physician received the American Cancer Society National Divisional Award at a recent membership dinner meeting.

A bronze medal and a citation for "outstanding contribution to the control of cancer" was awarded **Dr. R. A. MacDonald**.

The presentation was made by **Dr. Donald E. Stewart**, Crookston surgeon, president of the Society's Minnesota Division.

* * *

Dr. Lynn C. Stoker, Albert Lea surgeon, has been inducted into the Fellows of the American College of Surgeons.

* * *

Dr. T. R. Fritsche received the Harold S. Diehl outstanding physician award last October from the University of Minnesota Medical Alumni Association.

* * *

Dr. D. J. Dummer, New Brighton Clinic, has been re-elected to active membership in the American Academy of General Practice.

Venereal Disease A Serious National Problem, Says AMA

Venereal disease is spreading so rapidly that it now represents this nation's most urgent communicable disease problem.

VD is hitting particularly hard among teenagers and young adults, according to the American Medical Association.

The venereal diseases are infecting about two Americans a minute—3,000 a day, or 1,100,000 a year. Cases of infectious syphilis have almost tripled in this country in the past five years. More than a million

new cases of gonorrhea are developing annually.

VD can blind, cripple, and even kill.

The ravages of venereal diseases are all needless tragedy, says the AMA, because both syphilis and gonorrhea can be avoided. If contracted, they can be cured by prompt medical treatment.

The cure for both diseases—penicillin—has been available since 1943. Any family physician or public health clinic can administer

prompt treatment.

Venereal disease is caused by intimate personal contact.

Complacency, ignorance, and a free-and-easy attitude toward moral standards are partly responsible for the spread of VD; the increasing use of alcohol, especially among young people, also plays a role.

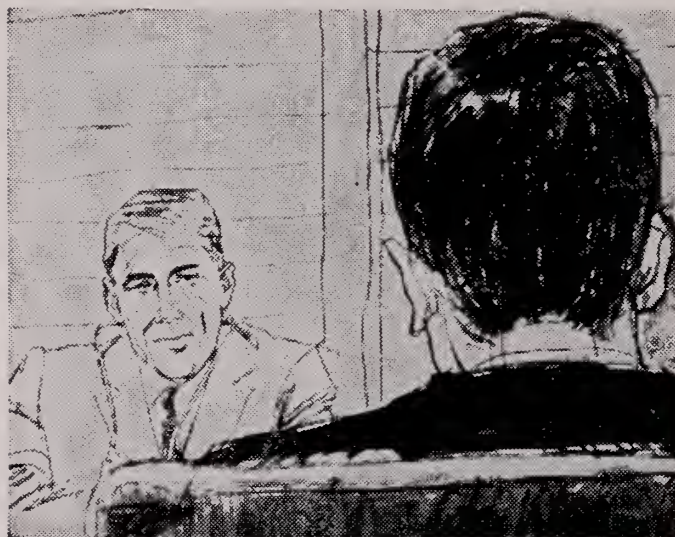
Authorities believe, however, that thousands of young people simply aren't aware of the dangers of VD. Once infected, they are complacent about treatment.

One of the first signs of syphilis may be a painless, ulcerating sore. Gonorrhea produces inflammation of the genital and urinary tracts, and a discharge of pus.

A person may contract syphilis and be unaware that he has the disease. After the first symptoms, the germs may remain hidden in the body for as long as 20 years before any damage is discovered. Then the person may become crippled, develop heart disease, blood vessel disease, blindness, or show mental symptoms. Even death may result from this hidden stage of syphilis.

If left untreated, gonorrhea may be responsible for arthritis, endocarditis, sterility, and blindness.

If a person suspects he may have contracted venereal disease, he should go to a physician immediately.



VD should be treated promptly by a physician.

Minnesota Medicine at a Glance

Diverticulitis of Pelvic Colon—Loffer and Bergquist

Page 1793

That diverticulitis of the pelvic colon can simulate gynecological disorders is well known but needs emphasis. The authors present a case in which a primary adenocarcinoma of the endometrium was complicated by a pelvic mass due to a ruptured colonic diverticulum. The true nature of things could only be suspected preoperatively but, once recognized at laparotomy, presented no special therapeutic problem.

Communication between Parents and Child—Burke

Page 1801

Communication, the sharing of feelings, ideas and ideals between parents and children, is the means by which children grow to adults and adults become mature. This quick view of the changing interactions between parents and children will be a good review for pediatricians, family physicians and for all physicians rearing children of their own.

Cardiac Resuscitation in a Community Hospital

Page 1925

Ho and Quattlebaum.

The experiences of a medium-sized community hospital in the field of cardiac resuscitation and defibrillation are presented.

A total of 119 patients were diagnosed as having had ventricular fibrillation or cardiac standstill over a period of three years. Satisfactory cardiac action was restored in 40 per cent. Twenty patients survived to be discharged, all of them well when they left the hospital.

The preparation, organization and procedure for diagnosis and treatment of cardiac arrest are reviewed.

Out of these Emotions

I am often asked, "How did you happen to study medicine?" Then I think of that strange "yellow day" in September of 1881, when the whole of the Eastern States were masked in an uncanny, sulphur-colored light—a mysterious, sinister light for which science has given no explanation.

It was on that day that I followed a rude country wagon moving slowly out from the Adirondack woods, over the long rough road homeward—its burden my brother's body. Somehow there was a weird, almost vaguely sympathetic fitness in the strange yellow light, toning with my grief and my despair.

I felt completely adrift, my whole plan of life in sudden and overwhelming chaos. The thought kept recurring; if I had known more of illness and the means of combating it, I might have been able to do more for him. Out of these emotions came the decision which set the course of my life.

I would become a doctor.*

Editor's Note: Alfreda Withington, after graduating from the Woman's Medical College of the New York Infirmary, spent her life in medical practice, living to the venerable age of ninety-one.

*Alfreda Withington (1860-1951) in *WHY WE BECAME DOCTORS*, edited by Noah Fabricant, M.D., 1954.

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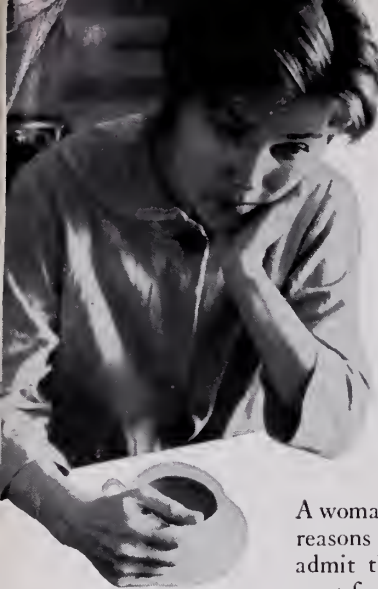


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Precautions: Limit dosage to smallest effective amount in elderly or debilitated patients (not more than 1 mg, one or two times daily initially) to preclude ataxia or oversedation, increasing gradually as



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Periodic blood counts and liver function tests advisable in long-term use. Cease therapy gradually.

Side Effects: Side effects (usually dose-related) are fatigue, drowsiness and ataxia. Also reported: mild nausea, dizziness, blurred vision, diplopia, headache, incontinence, slurred speech, tremor and skin rash; paradoxical reactions (excitement, depression, stimulation, sleep disturbances, acute hyperexcited states, hallucinations); changes in EEG patterns during and after drug treatment. Abrupt cessation after prolonged overdosage may produce withdrawal symptoms (convulsions, tremor, abdominal and muscle cramps, vomiting, sweating) similar to those seen with barbiturates, meprobamate and chlordiazepoxide HCl.

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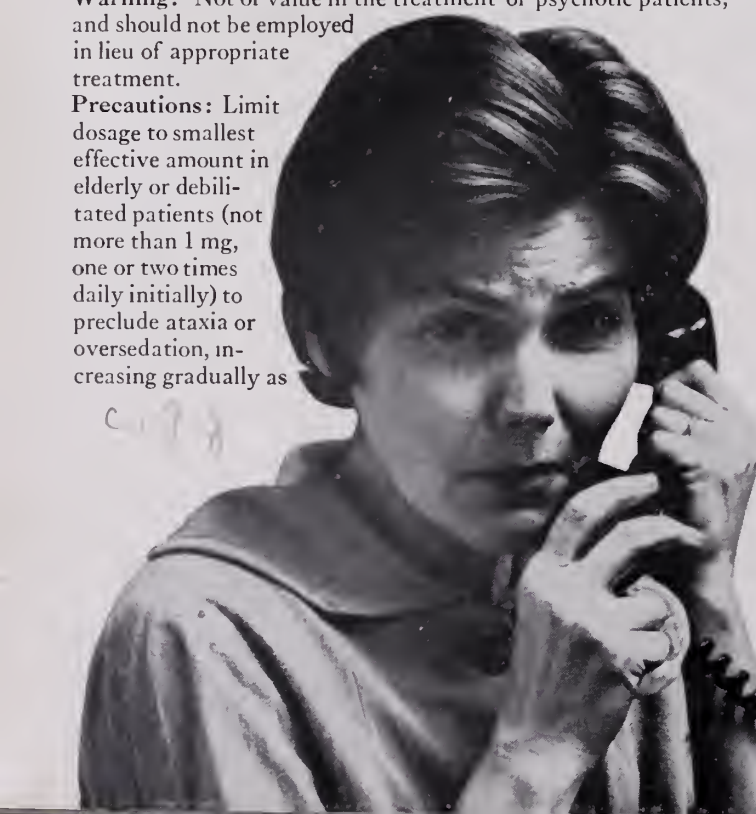
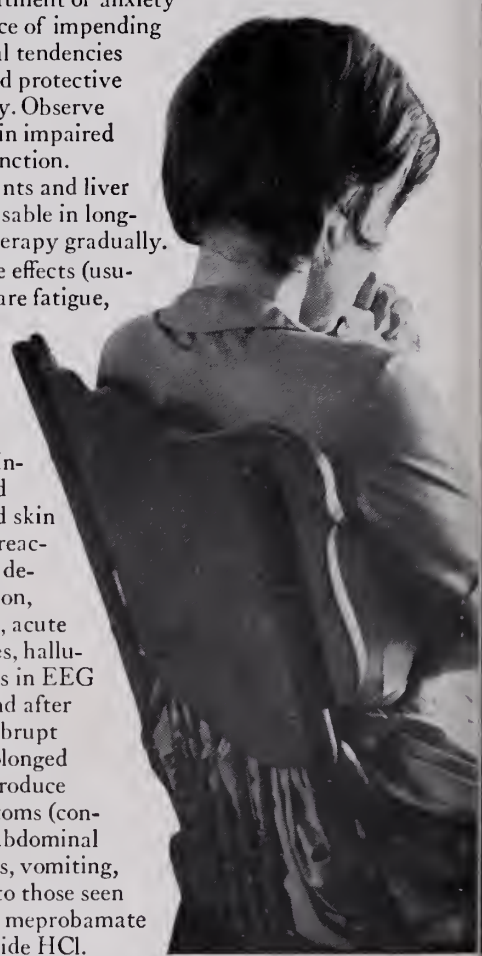
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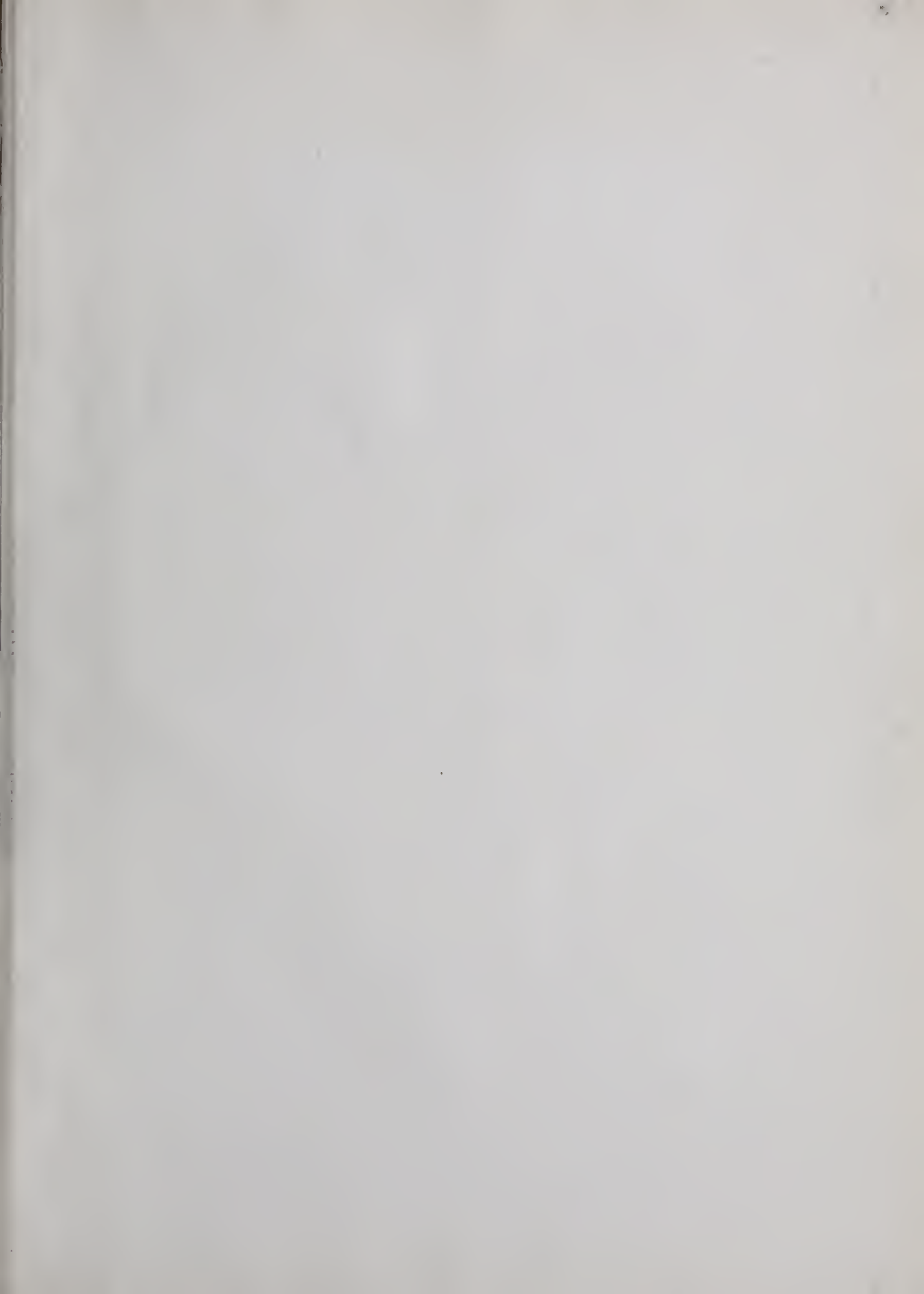
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